PATENT TERM EXTENSION AND PHARMACEUTICAL INNOVATION

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BEFORE THE

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INVESTIGATIONS AND OVERSIGHT

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PATENT TERM EXTENSION AND PHARMACEUTICAL INNOVATION

THURSDAY, FEBRUARY 4, 1982

House of Representatives,
Committee on Science and Technology,
Subcommittee on Investigations and Oversight,
Washington, D.C.

The subcommittee met, pursuant to call, at 10:15 a.m., in room 2325, Rayburn House Office Building, Hon. Albert Gore, Jr. (chairman of the subcommittee) presiding.

Mr. Gore. The subcommittee will come to order.

I would like to welcome our guests this morning and note for the record that we will hold the record open for a statement from the ranking minority member, Mr. Walker, who is unavoidably detained at the National Prayer Breakfast this morning. General Dozier was an honored guest there, and I think that the traffic coming from the breakfast has prevented Mr. Walker from being here right now. But we are going to hold the record open.

Let me say that we are going to try to keep that door open, because it is heating up in here. If some of our guests who are standing would like to take some of the seats on this side and this side of the first row, you are welcome to do so.

Today the Subcommittee on Investigations and Oversight continues its series of hearings on research and development prospects in scientific and high-technology fields. The subcommittee turns its attention in this hearing to the subject of patent-term extension for pharmaceuticals and the effects of such proposals on innovation in the industry.

Related to the question of innovation are the issues of equity in the application of the patent laws, effective patent life, and competition in the industry. Each of these corollary issues also has a direct bearing on the rate of innovation. We will hear testimony on these issues from the Office of Technology Assessment, which in addition to testifying about its previous work will discuss the results of a new analysis that I have personally asked be done. We are also pleased to have Commissioner Hayes of the Food and Drug Administration, and Deputy Assistant Secretary for Health Robert Helms here to present the views of the administration. Dr. William Wardell, who has worked extensively in the area of determining effective patent life, evaluating licensing trends in the industry, and other areas, and on whose work this legislation is largely based, will testify and update the work that he has done in the past. Testimony will also be presented by representatives of the Pharmaceutical Manufacturers Association and the Generic Pharmaceutical Industry Association.

The implications of patent-term extension for both consumers and the pharmaceutical industry are enormous. In dealing with an issue of such complexity, it is critically important for information to be complete. Because of economic as well as scientific factors, research and development in high-technology areas is highly dynamic. The Congress must stay abreast of these trends, particularly where there is a significant presence by the Government.

The patent-term extension issue has been explored previously by the Health and Environment Subcommittee, chaired by Congressman Henry Waxman. The Judiciary Committee's Subcommittee on Courts, chaired by our colleague, Mr. Kastenmeier, is currently considering legislation that addresses this subject. The purpose of this hearing is to expand upon the work of these two subcommittees, and to assess the issue from the perspective of pharmaceutical innovation. The subcommittee hopes that this hearing can complement the work undertaken by the other subcommittees, and that the information developed today will make a positive contribution to the debate.

I recognize my colleague, Mr. Shamansky.

Mr. SHAMANSKY. Mr. Chairman, I just wish to second your excellent statement. Our function is educational, and I think the public has a right to know all aspects of this very important legislation. Thank you.

Mr. GORE. Mr. Volkmer.

Mr. VOLKMER. No statement.

Mr. GORE. We would like to call our first witnesses, Mr. Norm Balmer, Project Director of the Patent-Term Extension Project with the Office of Technology Assessment, and Miss Donna Valtri, Assistant Project Director of the Patent-Term Extension Project at OTA.

In keeping with the tradition of this investigative subcommittee, I would like to swear all of the witnesses today. It is a practice that we adopt in all investigative hearings. So if you have no objection, if you would stand and raise your right hand.

[Witnesses sworn.]

Mr. GORE. Thank you very much. Without objection, the entire text of your prepared statement will be put into the record in full. We invite you to proceed with the presentation at this point.

STATEMENT OF DONNA VALTRI, ASSISTANT PROJECT DIRECTOR, PATENT TERM EXTENSION PROJECT, OFFICE OF TECHNOLOGY ASSESSMENT; ACCOMPANIED BY NORM BALMER, PROJECT DIRECTOR, PATENT TERM EXTENSION PROJECT, OTA

Ms. VALTRI. Thank you, Mr. Chairman.

Since my statement is fairly short I would like to just read it.

Mr. GORE. All right. If you could bend that large microphone toward you and pull it a little bit closer.

Ms. VALTRI. Good morning. I am Donna Valtri, an economist with the Science, Information, and Natural Resources Division of the Office of Technology Assessment. I served as assistant project director for the OTA study, "Patent-Term Extension and the Pharmaceutical Industry." I am accompanied today by Normal L.

Balmer, a patent attorney and project director for the study. I am pleased to testify on some of OTA's findings.

Our study examined many aspects of patent-term extension. Trends in pharmaceutical innovation were reviewed, and factors that appeared to have influenced these trends were identified in an effort to determine whether there was a correlation between changes in the individual factors and changes in the trends of pharmaceutical innovation. This approach was designed to provide a basis for assessing the effect of patent-term extension on pharmaceutical innovation.

Our study concluded that although patent-term extensions can encourage innovation through the incentives they provide to patentees, the evidence available neither supports nor refutes the position that innovation will increase significantly because of such extensions. There are two major reasons why OTA cannot be more definitive on this subject. The first is the lack of consensus among experts about how to measure innovation. The second is the inherent difficulty in quantifying the extent to which any individual factor contributes to the overall innovation rate.

The focus of my testimony today will be an explanation of these two areas of difficulty. I will first address the measurements of pharmaceutical innovation and then discuss the factors affecting innovation. The implications of extended patent terms for various members of the pharmaceutical industry and for consumers will also be discussed.

There is no agreement on an appropriate measure of innovation. There are many methods for measuring pharmaceutical innovation, none of which fully portrays innovation in the industry. Measurements of innovation have been made using new chemical entities (NCE's), all drugs (including products other than NCE's), only therapeutically important NCE's or drug products, sales volume of NCE's as a percentage of total sales, and several others. To complicate matters, some of these measures have been tabulated over differing time frames causing differing results. Further, it has been suggested that no measure of innovation can be adequate unless it takes account of the overall health improvements in society. Thus, each of the measurements of innovation is open to various interpretations. Let me briefly review these measurements and their possible meanings.

The most frequently used measure of pharmaceutical innovation is the number of NCE's introduced each year. As I mentioned, there is disagreement as to whether all NCE's should be counted or only those displaying modest or important therapeutic gain. If one chooses to count all NCE's, innovation has declined significantly since 1950, but has remained stable since 1962, when a more stringent drug approval process was adopted. If one counts only NCE's with modest or important therapeutic gains, innovation has remained relatively constant over the entire period. Thus, this seemingly straightforward measure of innovation gives sharply different results, depending on which data are selected.

Even if the results could be unambiguously determined, there would be controversy over the use of NCE introductions as a measure of pharmaceutical innovation. NCE introductions fail to reflect innovations resulting from new formulations, new combinations of active ingredients, or new uses for existing drugs. For example, of the 1,916 notices of claimed investigational exemptions for new drugs (IND's) pending at the Food and Drug Administration (FDA) on October 1, 1980, only 43 percent were for NCE's. In contrast to the two results using only NCE's to determine pharmaceutical innovation, the inclusion of all types of drugs approved by the FDA shows that innovation over the last decade was stable for several years with steady increases in more recent years.

There are several other methods for measuring pharmaceutical innovation, each with its own proponents. One could choose to focus on all drugs with important therapeutic gains, but in doing so one must look beyond NCE's. In 1980, of the 209 candidates judged by the FDA to offer important therapeutic gain, 86 were not NCE's. When this method is used, the rate of introduction of drugs with modest or important therapeutic gains has remained stable. One criticism of using therapeutic gain to measure innovation is that the determination of therapeutic value is a subjective matter and standards have varied over time. Despite the lack of consistent criteria, it is worth noting that each new drug that improves our health also increases the base against which the next drug is judged. Thus the rate of introduction of drugs with modest or important therapeutic gains has remained stable under increasingly difficult circumstances.

Trends in innovation also have been measured by NCE sales as a percentage of total ethical drug sales. The results of this measure indicate a decline in innovation. Since actual sales of NCE's have grown, this measure may only indicate that sales of other types of drugs are growing at a faster rate than sales of NCE's, rather than indicating a decline in innovation.

Still other measurements of innovation in the pharmaceutical industry have been suggested. The last one I will mention today is the average number of new drug submissions per FDA reviewer, which has more than doubled since 1971. It has been suggested that the annual approval rate might have been higher in recent years if more personnel had been available to review applications.

From the wide disparity in results, we conclude that interpretations of trends in innovation are highly dependent on the measures used and the time period being measured. To the extent that some more specific conclusion can be made, we find that by most of the measures we reviewed, innovation does not appear to be increasing. We did not pursue this further to determine the implications of a stable rate of innovation for health care.

Even if we were able to measure and agree on the rate of pharmaceutical innovation, we could not provide quantitative information about the effects of patent-term extension on innovation. Patent life is but one of many interrelated factors that affect industry decisions to undertake the research and development activities required to produce innovation. To date it has not been possible to isolate the weight of any of these factors, let alone understand the relative importance of patent life in the larger scheme of innovation. With this in mind, let me take a moment to explain what we do understand about the effect of patent life on innovation and the limitations of our knowledge.

The effective patent life is the portion of the 17-year patent term remaining after FDA approval.

Mr. GORE. Could I interrupt you?

Ms. VALTRI. Surely.

Mr. GORE. Try to move that second microphone over there, too. I fear that some in the back of the room may have trouble hearing you.

Ms. VALTRI. It has, on average, declined since the early 1960's, but because of problems of definition, the extent of the decline cannot be stated precisely. Many factors influence the length of effective patent terms, and some of these are changing: The duration of the FDA regulatory procedure may be stabilizing; and the average time between the filing and issuance of a patent application is increasing slightly as a result of a backlog of patent applications in the Patent Office. Combined, these two factors could slow the decline in effective patent terms in the future. Furthermore, FDA is now giving highest priority to the drugs that it believes will provide significant therapeutic advances; hence, these drugs may fare better than the average drug in the future.

For an understanding of the effect of patent lives on innovation, use of average effective patent lives has two major drawbacks. First, because the number of patented new chemical entities approved in any one year is small, an unusual FDA approval or patent-approval process for one drug may skew the average. Second, the average obscures the differences among various categories of drugs. The range of actual effective patent lives may therefore be more useful for assessing the influence of patent lives on drug innovation. A range can tell us if certain types or categories of drugs had particularly long or short patent lives. For example, calculations of the effective patent lives of the 1980 top-selling drugs indicate that the effective patent lives of the drugs with highest revenues ranged from 11 to 17 years.

Data are not available from which we could determine the effect that different types of patents may have on the calculation of effective patent life. A pharmaceutical product may involve several inventions such as the chemical itself, the process for making the chemical, and the pharmaceutical use of the chemical. These inventions may be the subject of separate patents, each of which may issue from the Patent Office at a different time. Because process and use patents are less likely to result in exclusive market positions for patent owners, calculations of average effective patent life are usually based on chemical patents.

In some instances, however, process or use patents can be an effective means for insuring exclusive market positions for products. An additional process or use patent can extend the patent protection for the product; thus, the effective patent life of the product would be longer than the effective patent life that had been calculated on the basis of the chemical patent. This might occur, for example, if a patented process were the only commercially viable method for making a product. Then, even though the chemical patent had expired, a competitor could not competitively manufacture the product until the process patent had also expired.

Let me now turn back to the discussion of factors other than patent life that play a role in pharmaceutical innovation. Some of these have positive implications for future innovation; others do not.

Since 1956, profits for research-intensive firms (those producing the majority of NCE's) have been stable and higher than profits for most other manufacturing industries. Research techniques have improved, and the competitive pressure for innovation among research-intensive firms has not diminished. Yet there is widespread belief that the return to research-and-development investment is declining and that R. & D. is becoming less profitable. Because data are insufficient to measure accurately the return to research investment, we have focused on the underlying factors influencing the returns. The major factors are the costs of R. & D. activities associated with each new drug, the total amount invested in R. & D., and the revenues and profits of the firms conducting research.

The average costs of R. & D. activities associated with each new chemical entity drug have been increasing rapidly as a result of inflation and more stringent and time-consuming testing requirements. Because of the time spent in obtaining FDA approval may be leveling off and new research techniques are being developed, these R. & D. costs should increase more slowly in the future.

Real growth has occurred in total expenditures for research and development in the pharmaceutical industry. The relationship between revenues and R. & D. expenditures has remained highly stable over the past 15 years. For the years 1965 through 1978, research expenditures averaged about 8.5 percent of total sales. The historic stability of this relationship suggests that trends in R. & D. expenditures may continue to track trends in revenues.

Revenues and profits are influenced by the competitive pressures exerted on drugs. The competition may be from other patented drugs, from nondrug therapies, or from generically equivalent drugs. Despite any decrease in the average effective patent term that may have allowed generic competition to enter the market earlier, the revenues and profits of research-intensive firms have thus far not shown any significant effect from generic competition.

However, governmental actions over the past decade could result in increased competition from generically equivalent drugs. Most States now have laws that allow or require generic equivalents to be substituted for brand-name drugs specified in prescriptions. The FDA has adopted procedures to facilitate approval of generically equivalent drugs. The Federal Government now bases its reimbursements for prescriptions paid for under medicaid on the lowest wholesale price of generically equivalent drugs. Furthermore, the Supreme Court has ruled that laws prohibiting the advertising of drug prices are unconstitutional.

Despite these governmental actions, which could encourage competition from generically equivalent drugs, barriers to the acceptance of these products still exist. Physicians, who determine the market for prescription drugs, tend to write prescriptions for the easily recalled brand-name drugs. Pharmacists fear they will be liable if they fill a prescription for a brand-name product with a generic equivalent that later causes injury. Furthermore, consumer preference can play a role. A generic drug that looks different in terms of size, shape, or color from the drug the consumer has been accustomed to using may be rejected in favor of the more familiar.

Thus the effect of competition from generically equivalent drugs on the revenues and profits of research-intensive firms in the future is uncertain. If this competition increased significantly, the revenues and profits of research-intensive firms could decline. The historic relationship between revenues and R. & D. spending suggests that under these circumstances R. & D. expenditures might also decline. There is also a possibility that the opposite effect could occur—additional competition from generically equivalent drugs could encourage research-intensive firms to increase their R. & D. expenditures in an effort to maintain their market shares through drug innovations. OTA found no historical analog that would assist us in distinguishing which of these possibilities is the more likely.

OTA cannot provide much information to assist in the legislative debate about the effects of patent-term extension on pharmaceutical innovation. Nonetheless, patent-term extension has some discernible implications for members of the pharmaceutical industry and consumers.

For the research-intensive firm, the potential for obtaining increased returns on R. & D. investment over the long term may provide incentive for undertaking R. & D. activities. Once extensions begin to run, some firms will earn additional revenues that could be reinvested in R. & D. programs.

The bulk of revenues generated by patent-term extension will accrue to a few firms that have developed financially successful drugs. The increased revenues may serve to reinforce their dominance in particular research areas and hence in the markets those firms serve. Therefore, other firms may be discouraged from entering these areas.

Since the economic incentives provided by patent-term extension will be greatest for drugs with high income potential, the tendency of firms to direct their research toward drugs with large markets will be reinforced. Research that is apt to produce economically marginal drugs may receive greater attention as a result of patent-term extension. However, patent-term extension will not affect research on drugs with potentially small markets because such research is likely to remain economically unattractive.

Patent-term extension poses risks for production-intensive firms. Their long-term revenues are determined by the remaining product lives of drugs coming off patent protection. Thus, although they depend on innovative new drugs to expand their product lines, in some cases, the product lives of drugs with extended terms may be insufficient to justify the entry of production-intensive firms into these markets at all.

Consumers will usually benefit if more and better pharmaceutical are developed. Pharmaceuticals often provide substantial savings over other forms of health care. On the other hand, drugs covered by extended patent terms will cost more than they would have if their patent terms had expired unless patent-term extension results in the introduction of enough new drugs to exert downward price pressure on the prices of existing drugs. Both the benefits and the additional costs that may result from patent-term extension will affect the elderly and the chronically ill more than other elements of society.

In considering these implications, it should be remembered that the drug innovation process requires years of prior research and development. Assuming that patent-term extension would apply only to new drugs, the effects of legislation on either costs or benefits for consumers or industry members should be minimal for a decade.

I would be pleased to answer your questions.

Mr. GORE. Thank you very much. I would like to note for the record the excellence of the work that you two have done at the Office of Technology Assessment. I noticed in reviewing the statements by the industry witnesses who will appear later today that people on all sides of this debate seem to cite OTA as the definitive authority on aspect after aspect of this question, and the fact that everyone on whatever side of the debate they take can find support in your work and cite it with such respect I think is a real compliment. In my judgment the Office of Technology Assessment has really earned its spurs so to speak over the last several years, and is one legislative innovation that has paid great dividends and has been of remarkable assistance to the Congress in understanding issues as complicated and complex as this one is.

Ms. VALTRI. Thank you, Mr. Chairman.

Mr. GORE. In your statement you discussed different measures of innovation and noted that by most measures innovation in the pharmaceutical industry appears to be relatively stable. You said two things. First of all, since the dramatic changes that occurred in the 1962 law, innovation, however you measure it, has remained stable. It has not declined since 1962, correct?

Ms. VALTRI. By most measures, that is correct.

Mr. GORE. Now—and that was when the efficacy requirements were added of course and the law was revolutionized. If you look at chemical entities with significant value, then innovation of those kinds of entity itself has remained stable since even before the 1962 law?

Ms. VALTRI. Yes; that is correct.

Mr. GORE. Now, should the subcommittee infer from that conclusion that the factors affecting innovation have also remained relatively stable over time?

Ms. VALTRI. I do not know whether that conclusion can be drawn. I think that the factors that have affected innovation over time have perhaps changed not in the character of the factors but in the weight that each of the individual factors has played. At times when it was very difficult, for example, to get good personnel, that situation may have affected innovation. I do not know that this is a fact, but at one point perhaps universities were not putting forth enough scientists. This factor and others may have ebbed and waned over the time.

Mr. GORE. OK. That is a balanced response.

It has been argued that one of the key factors affecting innovation is the effective patent life for pharmaceuticals and changes in this measure over time. Dr. William Wardell, who will testify later today, and Martin Eisman have written an article on this subject which you cited in your formal report to the Congress, yet in your testimony you indicated the difficulties inherent in attempting to gain a true indication of the effective patent life. Have you observed any weaknesses in the methodology or in the analysis conducted by Dr. Wardell?

Ms. VALTRI. I would not say there are any weaknesses in his analysis. I would say I may have gone about it in a different manner. I think Dr. Wardell has made a significant contribution to this debate. He has looked at average effective patent lives, and the only problem with that as I mentioned in my testimony is that the range of effective patent lives may tell us more about the effect that patent life is actually having on innovation simply because there are a very small number of NCE introductions each year, so that an unusual experience at the FDA or at the Patent Office may skew that average considerably.

Mr. GORE. So in other words, to take an example, if an individual—if you were trying to get an individual's average income and an individual was making $10,000 a year for 9 years, and then in the 10th year he won the State lottery and got $100,000, if you then said that that individual's average income was $109,000 a year, you would miss something. You would not get a true picture of what that individual's income pattern had been?

Ms. VALTRI. Yes; that is a good example of what one unusual occurrence in a stream of years can do to an average. The person that you cited has a normal pattern of making $10,000 a year, I believe you said, and if we were to average in this windfall again in 1 year and look at his average earnings over all the years with that included, we would skew the normal pattern of income for this man.

Mr. GORE. And to shift from the example to the question at hand, if you had 10 new chemical entities and you were looking at the effective patent life, and one of the 10 was put on the shelf by the pharmaceutical company and they expressed no interest in it for whatever reason, and as a result it had a zero effective patent life or a negative effective patent life simply because they had not done anything to get an effective patent life, then any average that included that exceptional time span would again obscure the true picture of what was happening; is that right?

Ms. VALTRI. That is correct.

Mr. GORE. Let me interrupt my questions to recognize my colleague, Mr. Walker, who has arrived from the National Prayer Breakfast.

Mr. WALKER. Thank you, Mr. Chairman. I apologize for being late. Given the nature of some controversy here today, it is probably a good thing that one of us went to pray.

Mr. GORE. You are not assuming that only one of us did, of course.

Mr. WALKER. Only in an official capacity.

Mr. Chairman, our hearing today is an important one because it goes to the very root of one of the major problems causing many of this Nation's current economic distress. The American drug industry has long been a world leader, but that position has been seriously eroded in recent years. One of the major reasons for that erosion has been a lowering of innovation within the drug industry. While there are a number of causes for the lowered level of innovation, we will be hearing witnesses today who will tell us that the prime cause of this problem can be directly traced to the lack of economic incentives in favor of innovation. These are due to the loss of nearly one-half of the patent protection, which is the right of any inventor, because of the slowness of the Federal Government in completing the required approval process.

Nearly 200 years ago Thomas Jefferson authored the first United States patent law. He was a man of great genius who invented many things himself, and he fully recognized that inventors needed both encouragement and protection. He said, "Ingenuity should receive a liberal encouragement." That encouragement was the 17-year patent term in which the inventor held the sole right to market his invention.

Today that encouragement is terribly diluted. For most drug inventors the process is a long, frustrating, and expensive one to guide a new drug from conception to approval. Every year scientists screen more than 126,000 chemicals for potential drug development. Of that number they will actually follow up on about 1,000. Of that number only about 16 will ever make it through the regulatory process and eventually appear in the pharmacy. Only one-tenth of 1 percent of all chemicals entering the process will finally be approved.

A pharmaceutical company will apply for a patent immediately after discovering a new chemical which is promising in case any of their competitors are on the same track. The Patent Office generally issues the patent about 2 years later. But now the potential new drug must pass through the regulatory process. That passage now averages more than 7 years. In fact, today the average effective life of the patent protection of a new drug approved this morning would only be 9.5 years.

The development of new drugs is also very expensive in terms of both time and money. The entire process, from the time the research commences until the FDA approves the drug for marketing, may take anywhere from 7 to 12 years. All of that time, except the first 1 to 4 years, is taken up by the FDA regulatory review process.

As the process has lengthened, the costs have risen sharply. In 1962 it cost roughly $6.5 million to develop a new product and bring it to the point of marketing approval. Today the total cost is at least $70 million. The drug companies find that they can no longer get the same amount of research from their research investment that they once did. While the industry has maintained the same historical rates of research investment—about 12 percent of sales in current dollars—inflation has doubled the costs of research. The result is that in real terms the industry is now able to accomplish only one-half what it did in 1960. This trend is mirrored in the reduction of new drug introductions. In the early 1960's, a $3.6 billion pharmaceutical industry with effective 16-year patent lives produced 53 new drugs each year, while in the late 1970's a $16 billion industry with effective patent lives reduced to only 10 years produced barely 18 new drugs a year.

Finally, Mr. Chairman, let me take a moment to comment on the support the concept of drug patent restoration has received. I have here editorials from the New York Times, the Washington Post, the Wall Street Journal, the St. Louis Post-Dispatch, the San Francisco Chronicle, and the Chicago Tribune. These newspapers represent a wide range of political opinion, but on this issue they all agree that drug patent restoration is an idea which deserves the immediate favorable attention of the Congress.

Mr. GORE. Will the gentleman yield, and without objection we will put those in the record at this point.

[The information follows:]

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19 Section 1 Friday, May 1, 1981

Where the patent laws don't work

Patents are intended to give investors and creators of a new product 17 years of exclusivity to reap a return on their investment and make a profit from their discovery before it can be copied freely by others. But for developers of new medical drugs, it hasn't been working out that way.

Today, the process of getting a new medication approved by the Food and Drug Administration (FDA) has become so complex that, on the average, almost half of the patent life of a drug now expires before the product can be put on the market. In some instances, a manufacturer has only three or four years left to sell a new medication before the patent runs out and it can be copied by competitors.

With less chance to earn back their initial investment — it cost an average of $70 million to develop a new drug in 1979 compared to $6 million in 1962 — pharmaceutical companies are less motivated to invest in research and drug development and increasingly inclined to shift to non-drug products. Drug companies introduced an average of 53 new medications per year between 1959 and 1962, but only an average of 18 per year between 1977 and 1979.

So Congress is considering new legislation that would stop the clock from running on the patent life of any product that must be reviewed and approved by a government agency before it can be put on the market. The bill would add to the remaining life of the patent the time elapsed between the initial application for classification as an "investigational new drug" and final FDA approval — up to a maximum of seven years. If passed, the new law would also help companies developing new chemical products, although government approval time is not quite as lengthy for these substances.

Some objections have been raised to the proposed legislation because it would lengthen the time until a drug could be copied by the developer's competitors and marketed as a generic product, presumably at a lower price. But in the long run, we all stand to benefit much more from the discovery and availability of new medications. It is far less expensive to treat patients with drugs than with surgery or long hospitalization, which may be the only alternatives. And one of the most effective ways to cut health care costs is to develop new medications. Enormous savings, for example, could be made if we had more effective drugs for heart disease, cancer, genetic disorders, respiratory diseases, and a long list of other ailments for which better treatment is urgently needed.

On the average, scientists now screen more than 10,000 possibilities for every one new medication that is eventually approved by the FDA and put on the market. The proposed legislation would provide some inducement to pharmaceutical companies to continue risking their time and money on such long shots.

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Wed., June 17, 1981

Extending Patents

THERE ARE ABOUT 40 pharmaceutical manufacturers in this country, many of them in the Bay Area, and they are doing better than $16 billion a year. They are rich and profitable but they are not as technologically innovative as they once were. They are introducing fewer new drugs each year because research that produces new drugs is on the decline. They say they don't get enough benefit out of the life of their patents to pay the way of more intensive product development.

In 1959, the American drug establishment introduced 65 newly patented drugs; last year, only 12. Obviously this trend is adversely affecting the general public through the loss, i. e., the non-appearance, of uninvented drugs that might benefit health, cure disease and save lives.

THE WAY TO TURN this around, the companies are telling Congress, is to give the innovator of a new drug the same 17 years' protection for the exclusive life of his patent that the inventor of a newly manufactured widget gets. Once granted a patent, an ordinary product can go right into production. Not so with drugs and chemicals that must undergo the process of review and approval by a government agency. This is ever lengthening.

Of the 12 new drugs introduced in U. S. pharmacies last year, five had been patented as long ago as the 1960s, the other seven in the first half of the 1970s. Result: the average patent life remaining when at last the drugs went to market was seven and a half years. Ten years had been chewed up in regulatory review.

THE DRUG COMPANIES are not seeking to avoid review and testing; they want a law that would add back onto the term of the patent the time lost in testing and approving the new product. Seventeen years' market protection is their demand, and we think it's fair and justified. The Senate Judiciary Committee has agreed to this unanimously.

Why doesn't the House Judiciary Committee do the same? Apparently because of organized consumer objections that patent extension is a rip-off with nothing in it for them, that the drug companies are already making lots of money (true) but don't need more investment incentives (clearly untrue), and that with long-life patents the companies will charge higher prices longer. Also true, but as the 17-year patent incentive brings more new drugs onto the market, product competition will prove once again to consumer advocates what they seem to overlook: that intensive research and innovation are the real price regulator — for drugs as for any other product.

SAINT LOUIS POST - DISPATCH SATURDAY, JUNE 20, 1981

Patently Fair To Drug Companies

A bill now under consideration in the U.S. Senate would give drug companies and other manufacturers of substances that come under regulatory review fuller use of patent protection. A patent gives the company or person obtaining it protection from duplicative competition for 17 years. For drugs and other such substances, however, much of the patent time is consumed in valid safety and efficacy review. The bill would restore up to seven years of patent life to a drug once it is through the review process.

In 1980 only 12 new drugs were approved; their average remaining patent life was 7 years, 5 months. The drug companies make a fairly persuasive case that the time devoted to regulatory review sharply curtails the patent's financial incentive for research and development. Since 1962 amendments to the drug law increased testing requirements — and hence lengthened the time between a drug's development and when it goes on sale — the introduction of new drugs on the market has steadily declined.

The opposition to the patent restoration proposal is largely economic. Some say that drug companies will keep prices high and that it will take longer for lower-priced generic drugs to be marketed. These arguments are not without some merit. But restoring patent life could spur more research and the development of drugs. And companies may spread the cost of recovering R&D money over the longer period, holding down the price to the consumer. Finally, there is the matter of equity. Patent laws provide 17 years' protection. Why should drug producers be denied that?

THURSDAY, MAY 28, 1981

THE WALL STREET JOURNAL
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Long Life to Patents

The words "patent law" can hardly be said to possess a life-or-death ring. Not compared to words like penicillin or Salk vaccine. Yet the recent impact of the patent law on the drug industry could well be inhibiting those very kinds of discoveries.

Patents are a bribe: If you invest your time and money on risky endeavors, society will reward your success by granting you a temporary monopoly. U.S. patent laws confer a monopoly for 17 years during which the inventor can, presumably, earn a rate of return that makes the investment worthwhile. Society gets a reward too, of course; it gets an invention it might not otherwise have had.

This bribe is crucial to the drug industry. It's very costly, very time-consuming and very risky to develop a new drug. Currently, the process takes about 10 years, costs $70 million and has a failure rate of 90%. The promise of patent protection kept things humming until, in 1962, the thalidomide tragedy convinced everybody that new drugs needed more rigorous testing. This, in turn, meant more time elapsed before drugs could be brought to market.

Thus, the length of time between patenting a drug and getting FDA approval gradually ballooned from about one year, pre-1962, to over seven years now. In other words, drugs making their debut today have less than a 10 year monopoly life—not 17.

The telescoping of effective patent life has reduced rates of return to drug research and development. Industry studies show that over the past two decades, rates have been sliced in half. Since new products need anywhere from 12 to 19 years to generate R&D returns above 8%, the current life span of less than 10 years looks especially grim. After all, prudent financial management could earn a bigger bang-for-the-buck by buying government long bonds. As it is, drug companies have been diversifying into businesses like cosmetics and salad dressings where returns are nearer to market.

Falling rates of return have, quite naturally, translated into falling R&D. The ratio of R&D to sales has declined from 13 in 1962 to 8 in 1979. Moreover, this decline is mirrored in the decline in the number of new drugs: In 1960, the $3.5 billion drug industry brought forth 50 new drugs; in 1980, a $22 billion industry produced only 12 new medicines.

Other than the obvious implications of this drying-up of R&D, we might note one particular ill-effect—the impact of health care costs. Drugs are amazingly cost-effective. Consider two examples. Tagamet, an anti-ulcer drug, saves millions of dollars in surgical costs a year and the advent of a new class of heart drugs, calcium blockers, (due out any minute) might totally eliminate coronary bypass surgery.

There is a simple way to help restore R&D incentive to the drug industry: guarantee the full 17-year protection by starting the patent clock ticking *after* FDA approval, not before. Companies need an assured time horizon to make investment decisions and they should, in the present cost climate, be able to count on a full 17 years. Such a guarantee would reduce uncertainty over expected returns and cash flows, and, we hope, create the incentive to cure our hay fever.

Both the House and the Senate have bills to restore 17-year patent protection to the drug industry. We know that congressional action on patent law reform will not excite the network news into prime-time coverage. But that doesn't make it unimportant and there is every reason to believe, as even the sternest free market economists do, that society's return on this kind of bribe is well worth the payment.

WEDNESDAY, MAY 20, 1981

The Washington Post

AN INDEPENDENT NEWSPAPER

Patently Fair

THE DRUG industry is said to be at the brink of a new age of medical breakthroughs. It now hopes to strengthen its chances for solid returns on its research investments through a bill reported yesterday by the Senate Judiciary Committee. The bill would assure the drug companies and other industries subject to regulatory review that the protection afforded by patent laws is not seriously eroded by the often lengthy period of testing and review required before marketing is allowed. This is a reasonable assurance to require, and the Senate should approve the measure.

For reasons we assume have nothing to do with the locust cycle, patent law deems 17 years the appropriate period for protecting inventors from copycats. Since 1972, when requirements for more rigorous testing of drugs were added to the law, the time required for such preliminaries has stretched from seven to 10 years. As a result, by the time a drug is ready for market almost half the patent life has elapsed.

Since drugs are very expensive to develop, the industry argues that the effective curtailment of patent life discourages new research. Against the arguments of consumer advocates that longer patent lives will increase drug prices by delaying competition, the companies respond that encouraging more research will increase competition and thus lower prices; that drugs, however priced, are far and away the cheapest form of medical treatment and that longer patent protection may discourage high initial price markups now needed for quickly recouping costs.

There are merits on both sides of the price argument. The drug companies, moreover, with their enormous and durable profitability, do not make anyone's list of neediest cases. But there are stronger arguments in favor of patent life assurance. One is simple fairness. If 17 years is the right period for protecting the exclusive rights of inventors, there is no reason why those subject to federal regulation should be denied it solely by reason of that regulation.

There is also the strong desirability of reducing unwarranted pressure on the regulatory process. You don't have to be in favor of mindless bureaucratic delay to recognize the tremendous importance of thorough testing of drugs before they are widely peddled as the latest miracle cure. Some risk may be unavoidable, but no one can want to increase the chances of producing deformed infants.

Stronger regulation not only has reduced that possibility, but it may also have had other beneficial side effects. The higher cost of introducing new drugs, it is said, diverted companies from trial and error research and from the marketing of slightly better products into the basic biological research that is now promising to produce real cures for ailments ranging from asthma to heart disease and cancer.

There are probably ways that the FDA could further speed up clearance of major drug discoveries without jeopardizing the testing process. But assuring drug companies of a substantial period of patent protection is a reasonable and fair way to avoid having the desire for such protection translate into an unhealthy pressure on the review process.

SATURDAY, MAY 23, 1981

The New York Times

Founded in 1851

ADOLPH S. OCHS, *Publisher 1896-1935*
ARTHUR HAYS SULZBERGER, *Publisher 1935-1961*
ORVIL E. DRYFOOS, *Publisher 1961-1963*

The Half-Life Patents

For reasons long since forgotten, Congress a century ago chose to set 17 years as the appropriate period for patent protection. To encourage bright minds and investors, any invention was promised exclusivity in the market for that length of time. But in recent years, without anyone intending it, Federal health and safety regulations have eroded the effective life of many patents. For some products, the exclusive marketing period has shrunk to less than 10 years. The system discriminates unfairly against some of the most important research-oriented industries.

Consider the case of new drugs. When a pharmaceutical company uncovers a promising compound, it generally files for a patent immediately and usually gets it within two years. But before the compound can be marketed, it must pass stringent tests of safety and effectiveness. The regulatory review, required to protect the public, can itself take seven or more of those patented years. So the average effective patent life for drugs dropped from 17 years in 1969 to 9.5 years in 1979. The meaningful patent life for pesticides is now down to 12 years.

This discrimination is clearly accidental. Perhaps the best of several remedies is embodied in legislation just approved by the Senate Judiciary Committee and awaiting hearings in the House. It would simply extend the patent term for each product to compensate for time lost in clearing regulatory hurdles, up to a maximum of seven years.

Some argue the change would stimulate more research, lower costs, assist small business, help universities and promote exports. Others fear higher product prices in the protected industries without any significant benefit.

But that debate seems beside the point. The central issue is fairness and uniformity. If 17 years is to be the appropriate life for a patent, then a patent should be meaningful for 17 years. And if there is reason to distinguish between one industry and another, that should be done directly, not by inadvertence. It would seem to make no sense to protect a toy for 17 years but an important drug or agricultural chemical for only half that time. What Government grants at the patent office should not be taken away by its regulatory arms.

Mr. **Walker**. It deserves support if for no other reason than basic fairness and equity. If the patent protection period should be meaningful for 17 years, then it should be meaningful for all patents for 17 years. The protections granted by the Patent Office should not then be taken away by regulatory agencies. How can we possibly defend a system that grants the inventor of the next hula hoop a full 17 years of patent protection, but will then give the inventor of the drug that conquers cancer after years of effort and the investment of tens or hundreds of millions of dollars only one-half that protection?

Mr. **Chairman**. I think that the record at this point should clearly show that I believe that there are serious problems concerning the role of OTA in this hearing. As the chairman is aware, I only learned yesterday that there was some data and analysis which was done by OTA for the chairman which was said to have a direct bearing on this hearing and on the issue at hand. When I requested that same analysis I was told that the analysis in question had been done for the Chair as an individual. When I then provided OTA with exactly the same data that the Chair had and requested a similar analysis so that I could determine for myself if the analysis was germane, I was first told that no written materials existed; and then that all such materials were in the hands of the committee. When my counsel pointed out to OTA that the minority had not seen or heard of any such materials, the OTA representative then called the chairman's office to get clearance to release the data.

I would also like the record to show that the chairman himself did make the materials available to me yesterday afternoon, and for that I thank him.

But this morning I opened my New York Times to discover that an OTA study released yesterday, and I am quoting, "found that the time a drug spends in the regulatory process was not a significant determinant of effective patent life." How can it be that yesterday when I asked for germane information I was told nothing existed—and yet the New York Times gets that "nonexistent" OTA report and it goes to the very heart of the issue at hand?

The issue at hand is credibility. And the credibility in question, at least in my mind, is that of OTA. This was a body set up to make a fair and impartial assessment of scientific and technical issues. There are dozens of groups, agencies, departments, and congressional staffs who can be called upon to do a partisan analysis. There are unlimited assets in this town to do a political hatchet job on data and make the results come out the way you want it to. But OTA was above that, or at least they were supposed to be above that.

Let me quote further from the New York Times article: "Representative Gore, who has previously attacked the legislation, is chairman of the House Subcommittee on Investigations and Oversight which will hold a hearing on the bill Thursday. Industry groups will have their first chance at the hearing to respond to the new study." Well, Mr. Chairman, that is just fine for "industry groups." But I want to ask—Just who does OTA serve? Do they only work for people who agree with their view on an issue? Do they only work for the majority? In this issue I can only say that they are clearly not impartial. This nonexistent study of OTA was given to the Chair. It was given to the media. But it was not given to those who might not agree with the results.

I would also like to say that yesterday, when I objected to this process, OTA suddenly claimed that "while there was nothing in writing" in their files, they would attempt to write up the results, and get them to me yesterday afternoon. I had directed that they be provided to the minority staff so that some analysis could be made before this hearing. Nothing was received before the close of normal business hours yesterday. A response, best characterized as too little, and too late, did arrive at the minority office overnight, but this morning hardly gives adequate time to make any kind of detailed analysis.

Mr. Chairman, I want the record to show that I object very strenuously to the OTA conduct in this matter. It is outrageous that an official request for highly relevant data in the possession of OTA should be denied to one side of an issue at the same time that it is being provided to the media. As the chairman well knows, I am more than willing to debate any issue with him. We have had some very interesting sessions in this committee. And I respect both his abilities and his views, although I sometimes do not agree with them.

But I want everyone here to understand that because of the conduct of certain members of the OTA staff in this matter, because of the actions of leaking a "nonexistent" report to the media after first denying its existence, and then procrastinating in providing it to possible opponents until it was too late for a meaningful analysis, and finally, because I have noticed subtle differences between the testimony being presented today and previous OTA statements and publications which shade the meanings toward what seems to be a predetermined conclusion, I cannot accept this OTA testimony as either fair or impartial. I think that it is a tragedy that OTA has allowed itself to fall into this position. For years they have worked scrupulously to be, like Caesar's wife, above suspicion. I trust that the day will come again when I will be able to listen to an OTA witness and believe that what they are providing is a truly impartial analysis of the data.

Mr. Chairman, in reviewing the witness list for today it also strikes me that the only fair way to handle this is to allow the witness who is representing the Pharmaceutical Manufacturers Association to have the opportunity to appear as the final witness of the afternoon, so that he may have the opportunity to rebut statements of the other witnesses. It also appears that he should appear alone. The Chair seems to have set up a number of panels today, which I agree is our normal procedure, but it appears obvious that that one position will surely be at odds with some of the other witnesses that we have. Therefore, I ask unanimous consent that the representative of the Pharmaceutical Manufacturers Association be permitted to testify last and by himself.

Mr. **Gore**. Are you through?

Mr. **Walker**. Yes, Mr. Chairman. That completes my statement.

Mr. **Gore**. Thank you. Let me——

Mr. **Walker**. I do have a unanimous-consent request pending.

Mr. GORE. Reserving the right to object, I will address that. I do not think there will be a problem with it. Let me respond, please. I think that there has been an unfortunate misunderstanding. The subcommittee did not request the additional analysis by the OTA staff. As an individual member, I did. I took it upon myself to request from the Pharmaceutical Manufacturers Association the data on patent filings and FDA approvals for all drugs approved since the epochal change in the law in 1962. Billions of dollars are at stake in this legislation, and there is very little understanding of what the facts underlying this legislation really are. I asked for information that I thought would provide a better understanding.

The Pharmaceutical Manufacturers Association responded that it would be too much work to get all that information, but that they will provide it for the year 1980. I said, fine. Jim White of my personal staff got information from the Patent Office, from the FDA, and, as an individual member, I requested the assistance of those experts at OTA in melding together the three data bases to provide me with a better understanding of what was happening in this industry.

OTA is charged with the duty to assist committees and to assist Members of Congress. The OTA staff members with expertise in this area analyzed the data, and at my request provided me with that analysis. A second request, as I understand it, was made by your office, Mr. Walker, yesterday afternoon. Now, OTA and its employees have been put in the center of a multibillion-dollar vortex, and I think their testimony and their work really stand on their own merits, and they have nothing to fear and nothing to feel bad about, because they have performed remarkably.

Their responsibility to honor my request for information carried with it some responsibility to allow me to use that information as I saw fit. When a second Member makes an identical request for the same information, that second Member is entitled to it. However, if an initial request is made which requires a period of 4 months to comply with, then an identical carbon-copy request for the same information, if it is complied with as demanded within 5 minutes instead of the 4 months that it took to respond to the initial request, then it seems to me that OTA's responsibility to the first Member has not been fulfilled.

I understand that OTA did attempt to comply with your request for the identical analysis by the close of business yesterday. I do not know what happened, if it came shortly after the close of business. I do know that contrary to the statement just made that those who disagreed with the analysis, the industry, were provided with a copy of the information before the close of business yesterday.

As for the matter of the document being leaked to the media, OTA did not leak the document to the New York Times; I did. As an individual member I requested the information to improve my understanding of the issue, and I provided it in response to a request from a reporter for the New York Times with the explicit understanding that it would not be released prior to the day of the hearing, and that was in fact complied with. So I think that the individuals at OTA who are in this vortex really have been the object of an unfair attack, and by unfair I do not wish to imply that it was intentionally unfair. I think it is based on a misunderstanding about the nature of the original request made to OTA.

Now, I would like to ask you, Mr. Balmer, before proceeding further, if you would like to——

Mr. **Walker**. Mr. Chairman, if you would yield?

Mr. **Gore**. Let me deal with the unanimous-consent request that is pending. We had intended to have the spokesman for the Pharmaceutical Manufacturers Association appear as part of a panel with the generic manufacturers, as well. We had invited the head of the Pharmaceutical Manufacturers Association to discuss this important issue, and I regret that he is unable to be here. I have great respect for him, and I am sure that his failure to appear is unavoidable. If my colleague wishes for Mr. Hutt, the lawyer for PMA, to appear separately, I see no problem with that. We will have Mr. Hutt as a separate witness before the panel from the generic manufacturers, and then we will ask——

Mr. **Walker**. Mr. Chairman, the unanimous-consent request was that they be permitted to appear last.

Mr. **Gore**. All right. We will have Mr. Hutt appear as a separate witness before the pharmaceutical—the generic manufacturers, and then we will ask him to come back and have a second bite at the apple, and at the conclusion of the generic manufacturers' testimony we will ask Mr. Hutt to join with panel and provide any rebuttal or criticism of the generic manufacturers' testimony that he sees fit.

Now, I will be glad to yield.

Mr. **Walker**. Mr. Chairman, that was not the unanimous-consent request, but in the spirit of fairness, and I want to be fair to the chairman's decisions, I think that is an adequate compromise, and I am certainly willing to accept that as a compromise position.

If you would yield?

Mr. **Gore**. Sure.

Mr. **Walker**. I think it is clear in the New York Times article that indeed you did release the information to the New York Times, because the article said so, but that was not the question that was being raised. The question being raised was that this was released as an official study of OTA, and the article also makes that quite clear. So OTA does have some responsibility, then, for the data that was presented, and that is my complaint, the fact that on the day that I was supposed to come to this hearing and was supposed to be prepared to debate the issue at hand, I was unable to get the information that obviously was in such form that the New York Times was able to print it this morning.

Mr. **Gore**. Will the gentleman yield?

Mr. **Walker**. We requested that information yesterday, and first were told that it did not really exist. Obviously it does exist?

Mr. **Gore**. Will the gentleman yield?

Mr. **Walker**. Be glad to.

Mr. **Gore**. The gentleman was not personally told that it did not exist?

Mr. **Walker**. My staff was told.

Mr. **Gore**. I think that is a true misunderstanding. First of all, it was not a study, and to the extent that the newspaper article described it as a study, it did not hone in on the distinction between a study and an analysis, which is an understandable oversight for those not fully versed in how OTA operates. It was an analysis provided to me as an individual. They gave it to me, and I believe what was told to your staff was that they had given it to me.

Mr. **WALKER**. No; I was told that there were no written materials that existed.

Mr. **SHAMANSKY**. Would both gentlemen yield for a moment?

Mr. **GORE**. Be glad to.

Mr. **SHAMANSKY**. Mr. Chairman, I was here on time, with all due respect to everybody, and I am interested in the colloquy, but I think the points have been established. I would appreciate greatly the opportunity of asking questions of the first witness, because I have to leave.

Mr. **GORE**. At this point—I will move to you in one second—at this point I think it is appropriate after all of this controversy that the analysis that I asked to be prepared for me be included in the record at this point. I would like to ask just two brief questions about it.

Mr. **WALKER**. Reserving the right to object on that, and I certainly will not object, but do I understand then that the analysis is going to be included in the record not as a study and not as an official report of OTA, but rather is going to be put into the record as an analysis of material that you personally sent to OTA and asked for their evaluation based upon the point of view that you were looking for?

Mr. **GORE**. No, no, no, no, no; I mean it is all right with me that it be designated as an official analysis rather than an official study, but this was not—I did not call them up and say, "Hey, give me some information to support a position in opposition to the patent-term extension." I said, "Tell me the relationship that appears in these numbers between effective patent life and innovation and what factors have an effect on that."

Mr. **WALKER**. Is this going to be put in the report as the official OTA position on this matter? I am reserving the right to object.

Mr. **BALMER**. Mr. Chairman.

Mr. **GORE**. Mr. Balmer.

Mr. **BALMER**. We would like to say something. You have discussed the matter, and we would like to at least point out some things as we see them——

Mr. **WALKER**. I reserve the right to object. I would like an answer to that question. Is this material before I allow it to be entered into the record going to be entered into the record as the official OTA position?

Mr. **GORE**. What are your preferences on that? Is there a review procedure that is required prior to designation of an analysis of this kind as an official OTA analysis?

Mr. **BALMER**. Up to this point OTA has only four official documents representing their position.

Mr. **GORE**. OK.

Mr. **BALMER**. That is the only official position of OTA on this matter. The first one was our testimony before Chairman Kastenmeier on July 22. The release of our report constituted the second one. The letter request from Mr. Walker which we responded to yesterday is the third. The fourth is our testimony today. Our testimony today is the official position of OTA. The materials which you have received prior to this time have not been considered an official position of OTA. In fact, they have been on a staff-to-staff basis. They have not been reviewed by our hierarchy within OTA, nor have they received blessing from our Technology Assessment Board.

Mr. GORE. All right. They will be designated as an analysis done by the OTA staff for me.

Mr. BALMER. Let me clarify some other matters for the record. First off——

Mr. WALKER. Well, reserving the right to object. I just want to make certain how we are putting this in now. We are putting it in as to how the materials will be entered as an analysis done for the chairman which does not represent OTA's official position; is that correct?

Mr. GORE. Which has not been formally adopted by the OTA board; correct?

Mr. WALKER. Thank you, Mr. Chairman. I withdraw my reservation.

Mr. GORE. Go ahead, Mr. Balmer.

Mr. BALMER. There has been a lot of discussion about the extensiveness of the analysis and there is an implication that it took us 4 months to comply with the request. In fact, the analysis which we conducted was a regression analysis done over the weekend using a computer which Ms. Valtri's husband has at home. It is a simple analysis. It was quick. It certainly did not take 4 months; it took a matter of a couple of days.

Second, there is no OTA study or analysis. OTA has not talked with the press. The discussion that appeared in today's New York Times came as just as much of a surprise to us as it did to you.

Let me further address or perhaps offer to the subcommittee our official response which went to Mr. Walker yesterday evening, and was delivered both to Mr. Walker's office and to Mr. Clement's office about 5:30 or 5:35.

Mr. GORE. And the first request for the information from Mr. Walker's office came when?

Mr. BALMER. We received the letter about 12:35 yesterday afternoon.

Mr. GORE. Five hours is not bad.

Mr. CLEMENT. The letter that they received was a followup on an earlier phone conversation some 14 or 16 hours before. They promised the information that was purportedly available.

Mr. SHAMANSKY. Would the gentleman yield?

Mr. GORE. Yes.

Mr. SHAMANSKY. The clock is going on, and I would like to ask the witnesses questions.

Mr. GORE. I would like to put it in the record at this point and ask a question about it. We have had all this argument. I would like to ask the staff to release the analysis.

[The information follows:]

Table 7

Calculation of Time Elapsed Between
Patent Filing and IND, IND and FDA Approval
For NCEs Approved in 1980 — Compound Patents Only

Brand Name	Date Patent Filed	IND Receipt Date	Date of FDA Approval	Time Elapsed: filing to IND	Time Elapsed: IND to Approval
				—— days ——	
				(2) - (1)	(3) - (2)
	(1)	(2)	(3)	(4)	(5)
Viroptic	9/18/63	7/17/74	4/10/80	3955	2094
Meclan	12/19/60	8/26/76	5/30/80	5729	1373
Cinobac	2/4/69	8/7/72	6/13/80	1280	2867
Meclomen	1/12/61	1/21/65	6/25/80	1470	5634
Vansil	5/29/68	9/11/70	7/23/80	835	3603
Calderol	3/17/69	6/24/73	8/5/80	1560	2599
Yutopar	2/25/65	4/22/71	8/29/80	2247	3417
Asendin	2/28/64	12/19/69	9/22/80	2121	3930
Zomax	7/26/67	7/22/74	10/28/80	2553	2290
Siseptin	6/27/68	1/22/73	10/29/80	1670	2837
Ludiomil	11/9/61	4/14/69	12/1/80	2713	4249
Spectrobid	9/7/71	11/14/76	12/22/80	1895	1499

Sources: Cols (1) and (3) – PMA-supplied data, November 6, 1981
Col (2) FDA-supplied data, July, 1981

Table 2

Dvalter, 11-7-81

Calculation of Effective Patent Life for NCEs Approved in 1980

Compound, Process, Use, and Composition Patents

Brand Name	Date Patent Issued	Date of FDA Approval	Time Elapsed	Effective Patent Life	EPL
			days	days 6205[a] – Col(3)	years (4) ÷ 365
	(1)	(2)	(3)	(4)	(5)
Viroptic	8/17/65	4/10/80	5350	855	2.34
Meclan	5/16/61	5/30/80	6954	(749)	(2.05)
Cinobac	6/13/72	6/13/80	2922	3283	8.99
Meclomen	4/11/67	6/25/80	4824	1381	3.78
Vansil	6/28/74	7/23/80	2217	3988	10.93
Vansil	9/2/75	7/23/80	1786	4419	12.11
Calderol	9/3/74	8/5/80	2163	4042	11.07
Calderol	1/18/77	8/5/80[1]	1295	4910	13.45
Yutopar	11/12/68	8/29/80	4308	1897	5.20
Asendin	8/1/72	9/22/80	2974	3231	8.85
Asendin	5/16/72	9/22/80	3051	3154	8.64
Zomax	8/14/73	10/28/80	2632	3573	9.79
Zomax	1/24/78	10/28/80[1]	1008	5197	14.28
Zomax	7/22/80	10/28/80[1]	98	6107	16.73
Sisoptin	9/23/75	10/29/80	1863	4342	11.90
Sisoptin	8/27/74	10/29/80[1]	2255	3950	10.82
Ludiomil	8/27/68	12/1/80	4479	1726	4.73
Spectrobid	3/25/75	12/22/80	2099	4106	11.25
Spectrobid	2/17/76	12/22/80	1770	4435	12.15
				Avg	9.2

[1] approval date not given; assumed to be same as approval date of compound. See Vansil, Asendin, Spectrobid and FDA-supplied data.

[a] 17 x 365; no accounting for leap years

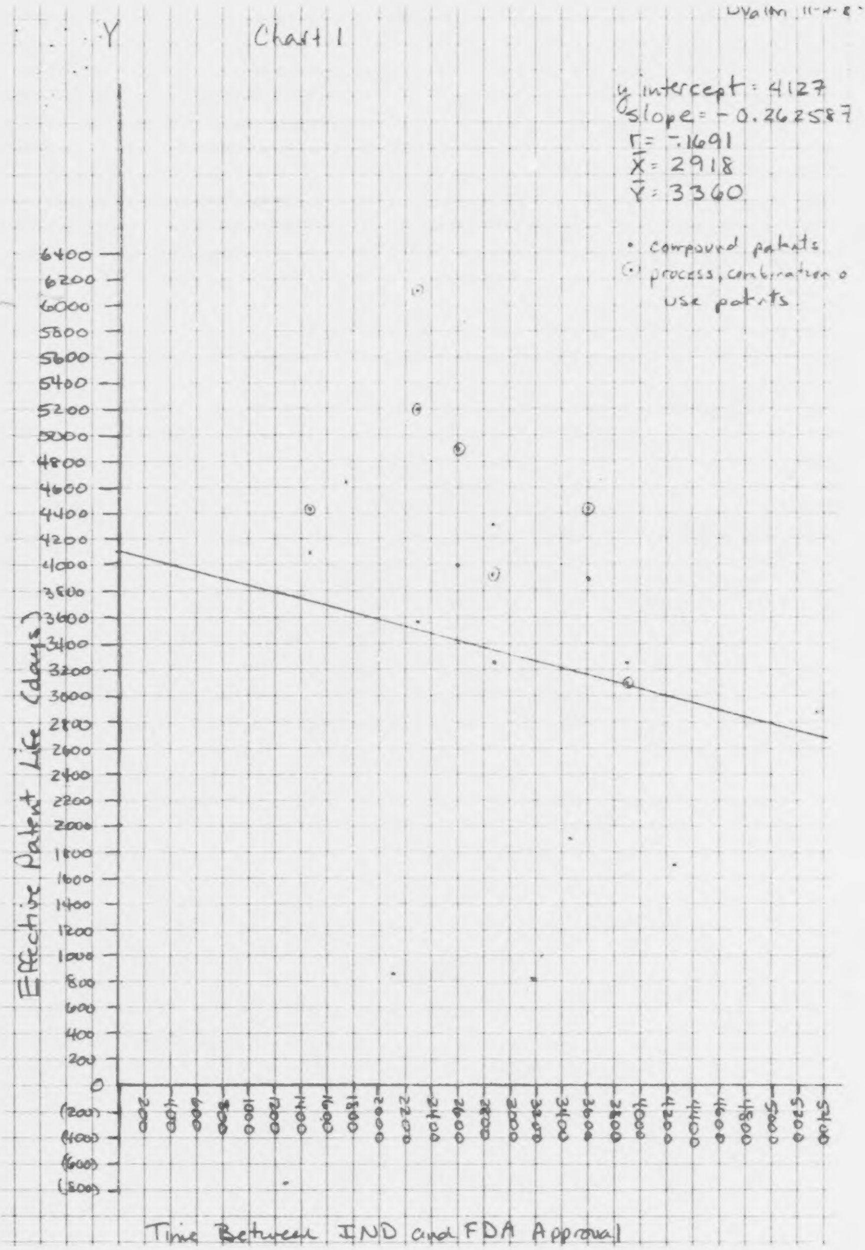
Table 3

DValtr. 11-

Calculation of Effective Patent Life If IND Had Been Filed 2 Years After Patent Application Date - for NCEs Approved in 1980

Compounds Only

Brand Name	Patent Filing Date	Proforma IND Date	Date Patent Issued	Pro Forma FDA App. Date	Time Elapsed	Effective Patent Life	EPL
		Col(1) plus 2 years		Col(5) of Table 1 + Col(2)	days Col (4) - Col (3)	days 6205 minus Col (5)	years Col(6) ÷ 365
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Viroptic	9/18/63	9/18/65	8/17/65	6/18/71	2131	4074	11.2
Meclan	12/19/60	12/15/62	5/16/61	9/19/66	1952	4253	11.7
Cinobac	2/4/69	2/4/71	6/13/72	12/4/78	2365	3840	10.5
Meclomen	1/12/61	1/12/63	4/11/67	6/12/78	4080	2125	5.8
Vansil	5/29/68	5/29/70	6/28/74	3/29/80	2101	4104	11.2
Calderol	3/17/69	3/17/71	9/3/74	4/17/78	1322	4883	13.4
Yutopar	2/25/65	2/25/67	11/12/68	6/25/76	2782	3423	9.4
Asendin	2/28/64	2/28/66	8/1/72	11/28/76	1580	4625	12.7
Zomax	7/26/67	7/26/69	8/14/73	10/26/75	803	5402	14.8
Sisesptin	6/27/68	6/27/70	9/23/75	3/27/78	916	5289	14.5
Ludiomil	4/9/61	4/9/63	8/27/68	7/9/75	2507	3698	10.1
Spectrobid	9/7/71	9/7/73	3/25/75	10/7/77	927	5278	14.5
						Avg	11.6 ~~[illegible]~~


Y
Chart 1
y intercept = 4127
slope = −0.262587
r = −.1691
X̄ = 2918
Ȳ = 3360
• compound patents
⊙ process, combination & use patents
6400
6200
6000
5800
5600
5400
5200
5000
4800
4600
4400
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
(200)
(400)
(600)
(800)
Effective Patent Life (days)
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
2600
2800
3000
3200
3400
3600
3800
4000
4200
4400
4600
4800
5000
5200
5400
Time Between IND and FDA Approval

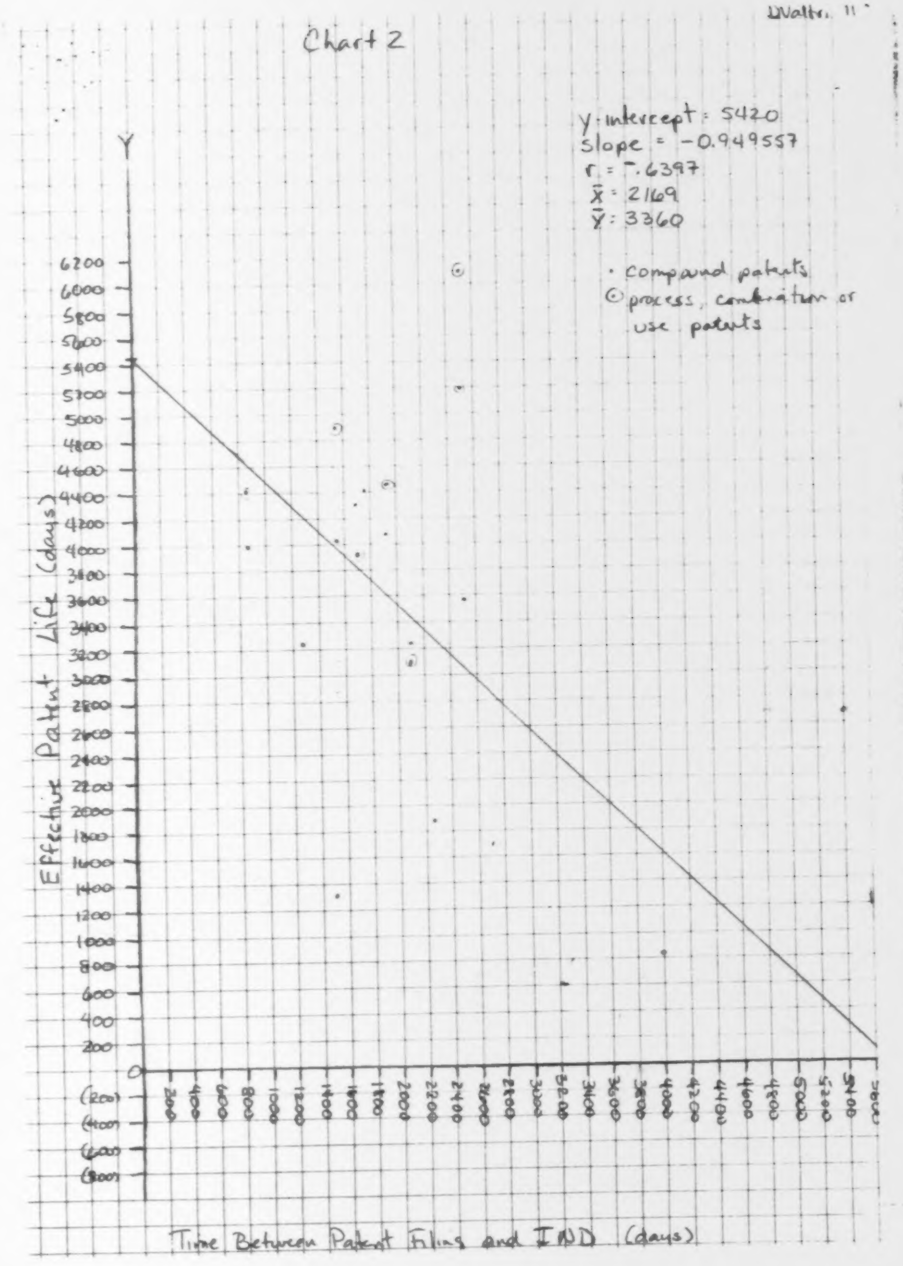


Chart 2
DValtr. 11
y-intercept = 5420
slope = -0.949557
r = -.6397
$\bar{x}$ = 2169
$\bar{y}$ = 3360
· compound patents
⊙ process, combination or use patents
Y
Effective Patent Life (days)
6200
6000
5800
5600
5400
5200
5000
4800
4600
4400
4200
4000
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
(200)
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1400
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2000
2200
2400
2600
2800
3000
3200
3400
3600
3800
4000
4200
4400
4600
4800
5000
5200
5400
5600
Time Between Patent Filing and IND (days)

Mr. GORE. Now, it has been described at this point, but let me just ask you to confirm that this analysis shows that statistically the Government regulatory review period does not appear to be a significant factor in determining the effective patent life of drugs approved in 1980? Ms. Valtri?

Ms. VALTRI. That is correct, Mr. Chairman.

Mr. GORE. Thank you very much. Mr. Shamansky.

Mr. SHAMANSKY. Ms. Valtri, I am very concerned about this because I have the terrible feeling that you asked the wrong question. Your study is directed toward for whatever reason the question of effects on trends in pharmaceutical innovation, which is very interesting to me, but I think it is irrelevant. I think you have stood up a straw man and knocked him down. To me the question is one of equity. How you gain innovation, which our Science and Technology Committee has been chasing that will o' the wisp all year. To this lawyer the question is, what is a patent? The patent is a granted monopoly. That is what it is about, and I find your information—I do not know why you did not address the question of equity. You say here your study examines many aspects of patent termination and you chose effects on pharmaceutical innovation.

With all due respect, that is irrelevant to me, because the patent itself is a monopoly granted to the originator that meets certain criteria. As far as I am concerned, the question is, does the patent have value, the same value in terms of time, to someone in the position of say a pharmaceutical house, as it does to somebody else where the delay may be caused by another Federal regulation? And I would like to ask, can you tell me why you chose innovation as the—as your standard as distinguished from something else?

Ms. VALTRI. Certainly. In the requesting letter from the chairman asking us to testify, he specifically asked us several questions that he would like to have us address; innovation was one of them. The other was the implications of this legislation for various members of the pharmaceutical industry and for consumers. We did however address equity, the issue you are concerned, with in our patent-term extension report. We do have a few pages on that in there. We did not deal with the subject in the report to a great degree, either, because the issue of equity is such a difficult one to determine.

Mr. SHAMANSKY. It is a very subjective thing. There is no way to quantify that. Beauty is in the eye of the beholder, correct?

Ms. VALTRI. Exactly.

Mr. SHAMANSKY. If I may go on, with respect to page 3 of your testimony, you say:

> If one chooses to count all NCE's, innovation has declined significantly since 1950, but has remained stable since 1962 when a more stringent drug approval process was adopted.

So clearly the Kefauver Act did have an effect here, when they had to prove whether or not a drug was effective?

Ms. VALTRI. Yes, sir.

Mr. SHAMANSKY. So in fact the effective patent life has been reduced, and it depends upon the particular drug, but objectively it has been reduced, has it not?

Ms. VALTRI. Yes; I think that is certainly fair to say.

Mr. SHAMANSKY. On page 6 of your testimony you say:

> Combined, these two factors could slow the decline in effective patent terms in the future. Furthermore, FDA is now giving highest priority to the drugs that it believes will provide significant therapeutic advances; hence, these drugs may fare better than the average drug in the future.

My question is, Why should a manufacturer gamble on that? It is like the toss of the dice, whether they decide to pick it up today or next week, the investigator got sick and so forth or he wanted to pick one as opposed to the another. There is no standard. There are other criteria by which you choose to do one or the other, apparently. The process can be long or short depending on innumerable variables. Whatever it is, it delays the effective life of the patent; is that correct?

Ms. VALTRI. That is correct.

Mr. SHAMANSKY. I ask, should the patent holder be penalized because they choose one as distinguished from the other? That is a question of equity, and not a question of innovation.

On page 7 you say:

> This might occur, for example, if a patented process were the only commercially viable method for making a product. Then, even though the chemical patent had expired, a competitor could not competitively manufacture the product until the process patent had also expired.

Is that not inherent in a patent? That is what a patent does.

Ms. VALTRI. Yes, sir. In that paragraph we were talking about how effective patent lives could be extended on one single product with the use of various patents.

Mr. SHAMANSKY. But that is implicit in the whole process.

Ms. VALTRI. Yes.

Mr. SHAMANSKY. OK.

On page 8 you mention about:

> Since 1956, profits for research-intensive firms (those producing the majority of NCE's) have been stable and higher than profits for most other manufacturing industries.

Certainly since 1956—that is a longer period back in this area, we do have medicare and medicaid and we are using—a lot of people are now having access to drugs who did not have access to them before. Certainly that would cause—there has been a much greater demand because there is an ability to pay for these products. So I am curious as to why that was in here.

Ms. VALTRI. The profits, if I understand you correctly, you are saying that the revenues of drugs have gone up.

Mr. SHAMANSKY. Yes, because more people have been able to buy them. That has nothing to do with the patent process, though.

Ms. VALTRI. Correct. And it has nothing to do with the profits in that context, either.

Mr. SHAMANSKY. Are you sure?

Ms. VALTRI. On an individual unit of drug.

Mr. SHAMANSKY. But the companies' overall profits have gone up because they are selling many more units.

Ms. VALTRI. The overall, the absolute value of the profits, the absolute dollar value that one has in one's pocket afterward as profit, yes, that has gone up. The percent that the profit is has not necessarily gone up because revenues have gone up.

Mr. SHAMANSKY. Well, I find it an economy of scale involved.

Ms. VALTRI. Depending upon the price of the drug sold and the quantities that are sold you could have different combinations leading to—you may for example sell 100 million units at cost and make no profit, or you can sell 2 units at a price that far exceeds cost, and make some profit.

Mr. SHAMANSKY. Later I refer to the question of orphan drugs; those that are for an illness which affects very, very few people. Clearly the manufacturers do not go into that because they cannot get their money back out. In a capitalist system that is not illegal.

Ms. VALTRI. Certainly not.

Mr. SHAMANSKY. I do understand the market approach on this thing.

Mr. GORE. Will the gentleman suspend briefly?

Mr. SHAMANSKY. Sure.

Mr. GORE. Once a year we have to get the committee budget approved. As senior staff of the committee I will have to go over there. We are going to have a recess for 15 minutes, and then we will reconvene at 11:30.

[Recess.]

Mr. GORE. The subcommittee will come back to order.

I will report to my colleagues that the subcommittee's budget for the next year was approved, a reasonable cut, one that I trust we can live with.

I would like to recognize my colleagues. Before doing so, I would like to get these other two charts up, if that is possible, and ask you to briefly explain them, Ms. Valtri, and then I will call on my colleagues.

The one that is up there now is an indication of the relationship between effective patent life and the time between the patent application and the IND filing; is that correct?

Ms. VALTRI. Yes, sir.

Mr. GORE. Now, the drugs that were approved by the FDA in 1980 are listed from left to right in order of declining effective patent life; is that correct?

Ms. VALTRI. That is correct.

Mr. GORE. And then next to each one is a graphical illustration of the time which elapsed between the application for a patent and the IND filing; is that correct?

Ms. VALTRI. That is correct.

Mr. GORE. Now, the usual time, the reasonable time that elapses between patent application and IND filing is around 2 years; is that correct?

Ms. VALTRI. I do not know that that is the reasonable time; that is what we have reported as the average amount of time that is required to perform the animal toxicity tests that are needed in order to attempt to apply for an IND at the FDA.

Mr. GORE. To take the most extreme example in 1980, Meclan, it took approximately 16 years from the time the company filed its patent and the time it filed for an IND; is that correct?

Ms. VALTRI. That is correct.

Mr. GORE. That is not the fault of FDA, is it? Do you know the circumstances that related to that?

Ms. Valtri. I do not know the circumstances that related to that drug.

Mr. Walker. Would you yield?

Mr. Gore. Yes.

Mr. Walker. The situation on Meclan was that there was no known use for the drug at the time it was developed, and so that would have some bearing on the statistics, is that not correct?

Mr. Gore. Yes; it would have some bearing on the company's enthusiasm for moving expeditiously through the filing procedure.

Mr. Walker. There would be no reason to file?

Mr. Gore. They did file. I think the record will show that where there is an attractive market for a drug, they will move it right along, and where there is a limited market or a market only overseas, then it will lie around. But they take all of them and lump them together and get the statistical result.

Mr. Walker. I think the filing took place after some years later a use was discovered for the drug, and so therefore that does impact on the statistics with regard to that particular drug. The filing came later, after they found a use for the drug.

Mr. Volkmer. Mr. Chairman, I know I have not been recognized yet. We have only gone an hour and 45 minutes. If it is permissible to have this kind of general discussion, I will start joining in.

Mr. Gore. Let me briefly present the charts, and then I will recognize my colleague.

The second chart adds a third factor. You have the time between the patent application and the IND filing in red, you have the effective patent life in blue, and the regulatory period in black. Now, whereas in the previous chart there was a very clear relationship between the elapsed time after patent application and before IND filing, it is clear from this graphic representation that there is no relationship between the effective patent life and the regulatory period. Would you as a statistician agree that the pattern shows no relationship between the regulatory period and effective patent life?

Ms. Valtri. No, sir.

Mr. Gore. Elaborate on your response.

Ms. Valtri. I would say that there is a relationship there. It is not as prominent as the relationship that we saw on the first chart.

Mr. Gore. Would you say that it is a significant relationship?

Ms. Valtri. No; it is not a statistically significant relationship.

Mr. Gore. So the relationship between the regulatory period and the effective patent life of a drug is insignificant?

Ms. Valtri. That is correct, it is statistically insignificant.

Mr. Gore. The third chart, if I could ask that it be presented—now this has an assumption built into it. The assumption is that the time taken between the patent application and the IND filing is 2 years. Now that figure was used because the OTA study indicated that 2 years was——

Ms. Valtri. The 1 to 2 years is the average time that it takes a drug company to perform the animal toxicity tests that are required to be performed before it can even ask for an IND at the FDA.

Mr. Gore. All right. The dotted blue bar graph section represents the additional patent life which could have been obtained if the time between the patent application and the IND filing had been 2 years, and in virtually every case, the effective patent life is extended dramatically. Now, this methodology is a regression analysis; is that correct?

Ms. VALTRI. That is correct.

Mr. GORE. To clarify the record, I used the figure 4 months earlier. I first requested the analysis in November and however long it took you to do it, that is what I was referring to. But your testimony is that this is a relatively simple analysis?

Ms. VALTRI. It is very simple.

Mr. GORE. If you have the data. If you have the data from 1962 up to 1980, you could fairly easily perform the same regression analysis on all of those drugs approved since 1962; is that correct?

Ms. VALTRI. That is correct.

Mr. GORE. Well, if we are going to pass a multibillion-dollar piece of legislation, it seems to me we ought to have such an analysis.

I recognize my colleague, the gentleman from Missouri.

Mr. VOLKMER. Thank you very much, Mr. Chairman.

Mr. GORE. You are welcome.

Mr. VOLKMER. I would like to ask first, what do we mean by effective patent life?

Ms. VALTRI. That is the term of the 17-year patent———

Mr. VOLKMER. 17 years?

Ms. VALTRI. It is the portion of the 17 years that remains after the FDA approves the drug and it is ready to be marketed.

Mr. VOLKMER. Wait a minute. The portion of 17 years?

Ms. VALTRI. That is correct.

Mr. VOLKMER. That is all I want to know. A portion of 17 years. That is very important, because on all your charts as I see it you start with patent application, do you not?

Ms. VALTRI. No, sir.

Mr. VOLKMER. What does that say up there, between patent application and IND filing? Take the other chart down, somebody. Patent application and IND. Now, patent application does not start the 17 years.

Ms. VALTRI. That is correct.

Mr. VOLKMER. Therefore, you are comparing apples and oranges.

Ms. VALTRI. No, sir, I did not compare the time period. The effective patent term that is listed on those charts, the blue lines, represents the time after the patent was issued.

Mr. VOLKMER. That is not the point. You are missing the point. I hope you are not that dense. Let us look at it again.

Ms. VALTRI. All right.

Mr. VOLKMER. Patent application. Let us take the first drug you have on the chart there. That is Siseptin. The application was actually filed on June 27, 1968.

Ms. VALTRI. Yes.

Mr. VOLKMER. The issuance of the patent and the patent life started on September 23, 1975. Now in your chart, you took the period starting in 1968. You did not take the period starting in 1975.

Ms. VALTRI. The blue line starts in 1975.

Mr. VOLKMER. But the patent application was 1968. That is the point. You are putting down 1975 instead of 1968.

Ms. VALTRI. The red line represents 1968. The blue line starts at 1975.

Mr. VOLKMER. The blue line started in 1975 on Siseptin?

Ms. VALTRI. Correct.

Mr. VOLKMER. Then if the blue line started—put the second one up.

Mr. GORE. I think it is the first one. Take that one down.

Mr. VOLKMER. That blue line is from 1975, 0 to 12. 1975 started 17 years. Where is the 17 years?

Ms. VALTRI. The 17 years is granted to a product by law. There are a number of things that affect the actual number of years a product will have as its effective patent life. In this case we have a number of variables that appear to be affecting how much out of that 17 years the product will end up with.

Mr. VOLKMER. No; wait a minute. You told me the red line is before the 17 years starts, but you are taking the red line off of the 17 years.

Ms. VALTRI. No; I did not take the red line off the 17 years.

Mr. VOLKMER. Add up. How many years do you have for Siseptin?

Ms. VALTRI. They should not necessarily add up to 17. If they do, it is by coincidence.

Mr. VOLKMER. I know they should not, but they do. And that is the problem with your chart.

Mr. GORE. Would my colleague yield?

Mr. VOLKMER. No; I will not yield, because the graph is not worth the paper it is printed on.

Mr. GORE. There is a simple explanation.

Mr. VOLKMER. I have had little time. I will not yield. If you start from the time the patent is issued and not from the time of the patent application, which is actually the patent life period, the 17 years, are you telling us that the period of regulatory process by FDA from the time of IND filing, the time of NDA approval has no impact on the patent life, marketing life of that patent?

Ms. VALTRI. What the analysis shows is that in 1 year—a regression analysis looks at the relationship between one variable and the other.

Mr. VOLKMER. And you left out the other, and plus you started at the wrong time.

Ms. VALTRI. It calls one variable the dependent and the other the independent. In both of the regression analyses that we did, the independent variable was the effective patent life. We wanted to see how that depended on the other variables. We looked at two: The regulatory period, to see how effective patent life depends on the regulatory period; we looked at the time taken between patent application and regulatory filing.

Mr. VOLKMER. But the patent life does not start until the patent is issued, not the time of the patent application.

Ms. VALTRI. You are correct. The patent process and the FDA process are independent processes.

Mr. VOLKMER. And the patent life does not begin until the patent is issued.

Ms. VALTRI. That is absolutely correct.

Mr. VOLKMER. Therefore the 17 years do not begin until the patent is issued.

Ms. VALTRI. That is correct, also.

Mr. VOLKMER. If an IND filing is made before the patent is issued, what difference does it make between the time of patent application and IND filing? Answer me that.

Ms. VALTRI. The patent can issue at any time. It may issue from the Patent Office during the period——

Mr. VOLKMER. You are not answering the question. I know that. You are evading the question.

Ms. VALTRI. Perhaps I do not understand the question, Mr. Volkmer.

Mr. VOLKMER. Let us put it this way. I am trying to make it very simple. If I file an application for a patent on January 1, 1970, and the patent is not issued until January 1, 1975—got it?

Ms. VALTRI. Yes.

Mr. VOLKMER. In the meantime I have filed my IND on January 1, 1974.

Ms. VALTRI. All right.

Mr. VOLKMER. Now what difference does it make in the patent life, the fact that I waited from January 1, 1970 to January 1, 1974 to file my IND?

Ms. VALTRI. Because the sooner you file the IND the sooner you begin the regulatory process and the quicker you get your product to market, and the patent life all this time is ticking away. So the quicker you are in these successive steps, the more patent life you may have at the end.

Mr. VOLKMER. You are saying if I file the IND sooner and if I get my patent—I will turn it around. I file my application on January 1, 1970 again. I do not get a patent until January 1, 1990, for some reason or other. In the meantime I have filed an IND on January 1, 1980. I get my approval on January 1, 1990. Under your analysis, I have delayed my patent by 10 years and yet I have not delayed it by one penny, one marketing time, but both of them came at the same time. The patent in 1990, FDA approval in 1990. I got my 17 years, have I not?

Ms. VALTRI. Absolutely.

Mr. VOLKMER. But under your analysis I delayed it 10 years because on January 1 I made my application, 1970; I did not file my IND until January 1, 1980, 10 years later.

Ms. VALTRI. Do you have a copy of our report?

Mr. VOLKMER. I sure do. Answer that. Under your use of that graph, answer whether I have not delayed or lost 10 years of my time. That is the 10 years in the red.

Ms. VALTRI. Maybe I can make it clear if I could direct you to a chart that we have in our report on page 13. Do you have a copy of that?

Mr. VOLKMER. I have looked at that chart.

Ms. VALTRI. As you can see from the chart, the drug development process, discovery, preclinical stage, the testing that has to go on at the FDA, the filing of the IND, all of these are completely independent from the patent process. The patent can be applied for and is usually applied for as soon as a drug is discovered. The patent may issue a number of years after that, or may issue quite close to the patent application. Things vary because of the patent law, not because of the drug approval process.

If the patent issues during the stage of IND to NDA approval, that is the regulatory period, the drug company can still not put that drug on the market until that approval is gained. Now, if the patent issues at an earlier time, independent of the process, and the company is not ready to go to the FDA, then the drug still cannot be put on the market. So they are completely independent processes.

Now, in this analysis, what we did was we said what does effective patent life depend upon? There are a lot of factors that are going on here at the same time. The patent approval process, the FDA approval process. We know that it takes a certain amount of time for a drug company to get to the IND stage. We know they have to do some toxicology tests, we know that oftentimes they have to license a drug. These things require a lot of time for negotiations. They have to be clear on their own that they actually have a drug that they are willing to make an effort with. These things take time.

We tried to see if there was any relationship between the eventual effective patent life that may be had on a drug after the FDA approved it and that time period between getting the patent application and starting the process of FDA approval, because clearly the FDA approval process inhibits the drug from getting to the market. One cannot market a drug until that approval has been gained. Because patent applications are generally filed very early—as soon as the company knows that they have something that might turn out to be a useful drug, they file it right away in case one of their competitors might also be working concomitantly on the same type of drug therapy—sometimes it takes a very long time to get through both the preclinical toxicology tests and the FDA approval tests. Nothing can happen until the FDA approves everything.

So we tried to describe the relationship between the actual regulatory period itself and the period before, because certainly the effective patent life stems from whenever it is that the patent may issue to the end of the patent. And what we found was for only 1 year, that in 1980 there seemed to be a rather distinct relationship between whether a company started the FDA process quickly and the eventual effective patent life. Further, we found that the regulatory period involved had some effect on effective patent life. That certainly explains some portion of it, but was not as explanatory a variable, as significantly explanatory as the first.

Mr. VOLKMER. Now that is a nice explanation. But I still do not believe that it refutes what I have said, and I would like to point out one other thing that you have not said in this process is that in this same year on these same drugs in the past that the IND was filed either before, except for, I think, three out of the instances, before the patent was ever issued.

Ms. VALTRI. Yes; that is often the case.

Mr. VOLKMER. Yes. And so on the patent life the delay, in my opinion, did not have that much—I would like to go back to your original statement, and then I am going to quit. Let us go back to what we are here for, and that is innovation, because I do not think you have mentioned whether this had anything to do with innovation:

> Our study concluded that although patent-term extensions can encourage innovation through the incentives they provide to patentees, the evidence available neither supports nor refutes the position that innovation will increase significantly because of such extensions. There are two major reasons why OTA cannot be more definitive on this subject. The first is the lack of consensus among experts about how to measure innovation. The second is the inherent difficulty in quantifying the extent to which any individual factor contributes to the overall innovation rate.

That is your statement word for word.

Ms. **VALTRI**. Yes.

Mr. **VOLKMER**. You stand by that?

Ms. **VALTRI**. Yes, sir.

Mr. **VOLKMER**. Then you are not saying according to your study that the pharmaceutical manufacturers are responsible for no innovation?

Ms. **VALTRI**. No, sir.

Mr. **VOLKMER**. Thank you.

Mr. **GORE**. That statement was made of course before you had available to you the information that I supplied and before the staff analysis of this data; is that correct?

Ms. **VALTRI**. That is correct.

Mr. **GORE**. All right.

Mr. **VOLKMER**. May I ask one more question while you are waiting, Mr. Chairman?

Mr. **GORE**. Yes. Very quickly. We have Dr. Hayes, who has a busy schedule.

Mr. **VOLKMER**. You realize, we are talking about the patent application period, that the legislation, patent restoration legislation does not attempt in any way to give or apply to the period between the patent application and the IND filing?

Ms. **VALTRI**. Yes, sir, I am aware of that.

Mr. **VOLKMER**. It does not have any effect on it whatsoever.

Ms. **VALTRI**. Right.

Mr. **GORE**. I recognize Mr. Walker.

Mr. **WALKER**. Thank you, Mr. Chairman.

You have talked about the amount of patent life lost by companies due to the time lapse between the patent issue date and the IND filing date. Are you suggesting in any way that companies intentionally diminish their patent lives by delaying their IND filings?

Ms. **VALTRI**. Certainly not.

Mr. **WALKER**. There would not be any motive for them to do that?

Ms. **VALTRI**. No.

Mr. **WALKER**. Are you aware that H.R. 1937 does not speak to this issue?

Ms. **VALTRI**. I am aware of that.

Mr. **WALKER**. So in other words a lot of the figures that we are dealing with here about the time between patent application and IND filing have absolutely nothing to do with H.R. 1937; is that correct?

Ms. **VALTRI**. What we were attempting to do here, sir, was look at the causes for the decline in effective patent life. It has been suggested in the debate that the cause for the decline in effective patent life has been the regulatory process, specifically, the time that it takes to go through in the regulatory process. This was an attempt to see for 1 year if that were actually true. And what we found was that while the regulatory period did, in fact, have some effect on the eventual effective patent life, we also found that the delay between patent application and IND filing also had a more significant effect.

Mr. **Walker**. But that is really not germane to the argument here, because the only thing that the legislation deals with is the regulatory time. That other time fit into the argument anyhow, because ultimately the regulatory time is the only thing that is going to be impacted on by H.R. 1937.

Ms. **Valtri**. Correct, H.R. 1937 only deals with the regulatory period.

Mr. **Walker**. While statistically figures might be fine to look at, they do not have any bearing on the discussion that is going on within the field at the present time.

Ms. **Valtri**. I think I would disagree with that. I believe they do have a bearing on the discussion. As I understand the legislation, and perhaps you can educate me on this further, as I understand the legislation it is an effort to remedy the cause for effective patent life decline.

Mr. **Walker**. It is an attempt as I understand it—it is an attempt to assure that those places where the Government impacts on the process that we do not take away at the other end of the spectrum. It does not solve all the problems. I do not think that there is any contention that it solves all the problems in the process, but it does solve the problem with regard to where Government is adversely impacting within the process, and it will not end up raising the total life of patents to 17 years if it is passed. In fact, it would suggest otherwise, and I have a chart here that has been developed, I think, which will clarify the fact that even with the patent life extended by H.R. 1937, that really taking the same data that you used in your study it will make it instead of 17 years about 13.1 years. Obviously it does not remedy the whole problem, it only remedies a portion of the problem, but it does appear based on the data which is in that chart that it would raise the effective patent life from 7.4 years to approximately 13.1 years. Is there anything in your data that would refute that particular figure?

Ms. **Valtri**. Nothing at all.

Mr. **Walker**. And so in fact your data would agree with the fact that for that period of time, in other words the addition of approximately 6 years there, that H.R. 1937 would help extend patent life for that period of time?

Ms. **Valtri**. Yes, sir. Our data also show that with expeditious filing of an IND that you could change for the same year the average effect of patent life of those drugs from 7.4 years to 11.6 years. So there are a number of ways to increase effective patent life.

Mr. **Walker**. So you are saying if you put your figures with regard to IND filing together with the figures that are in—the attempt that is being made in H.R. 1937, then you would come closer to the 17-year total?

Ms. VALTRI. No, sir, they would be different. I am saying that you can remedy—you can get more effective patent life by adding back years that were taken in the regulatory process and also by adding back years taken by the company between patent application and IND filing, either one.

Mr. WALKER. The problem I see with what you are saying is that to some extent you are making some assumptions that I am not certain can be entered into the process. For example, you said that a company could reduce its loss of patent life if it could file its IND within 2 years after filing the patent application. Have you talked with FDA officials to find out if that is feasible?

Ms. VALTRI. We have talked with FDA officials, drug companies, generic firms. We have talked with everyone, I hope, in the industry who would have a relevant comment on it. The time taken to file an IND application is approximately 1 to 2 years.

Mr. WALKER. In other words, though, then your 2-year timeframe is what you are saying is operative?

Ms. VALTRI. That is the average; yes, sir.

Mr. WALKER. That is the operative average right now. You know the problem becomes how then is that assumption going to fit with your figures if somehow a change there is going to extend the patent life, because you are suggesting a 2-year base.

Ms. VALTRI. Certainly a change in that assumption would change the results. If animal toxicity tests were taking quite a bit longer than 1 to 2 years on average, that would change the results.

Mr. WALKER. You are not suggesting we cut back on those tests?

Ms. VALTRI. No, sir.

Mr. WALKER. You are not suggesting that we reduce testing periods in terms of finding out whether or not the drug is safe for humans?

Ms. VALTRI. No, sir.

Mr. WALKER. I just want to look again there at the chart. The average period lost on a patent because of pre-IND work was 1½ years, if you take a look at those same drugs that were in your charts. I just want to make certain that what we have here is consistent with what you are saying. Does that seem reasonable to you based upon your work, that in fact the timeframe there is 1½ years?

Ms. VALTRI. Yes, I believe that is correct.

Mr. WALKER. In other words, that goes along with what you just said?

Ms. VALTRI. Yes.

Mr. WALKER. And that the bulk of the patent loss occurred during the FDA period? If you take a look there that the bulk of the loss was 8.3 years.

Ms. VALTRI. Excuse me.

Mr. GORE. Will the gentleman yield? I believe there is a misunderstanding about the 1½ years. That is the period between the filing of the patent and the issuing of the patent, and another variable in this whole process is the amount of time——

Mr. WALKER. It is the time between the patent—issuance of the patent to the IND filing.

Ms. VALTRI. I am sorry. It is very difficult for me to read that chart from here. I misspoke. You have up there the period from patent issuance to IND filing, and what I testified was the period from patent application to IND filing.

Mr. **Walker**. But the application period does not relate to anything that we are talking about here. The patent application does not really start the 17 years. The 17 years do not start until you actually have a patent issued; is that not correct? The point I am trying to make is what we are trying to do is reduce or talk about that 17-year period, is that not correct? I mean that is what most of this is all about, and whether or not that allows sufficient period to make companies innovative and so on. That is what this subcommittee is all about. It seems unuseful to me—I am not sure if that is a good word. We may have to correct that for the record. It does not seem very useful to me to start with something that does not relate to the final figures that you are coming up with.

Ms. **Valtri**. Earlier you said the legislation tried to address what impact the regulatory period had on the patent life. We tried to see what the impact of the regulatory period was on patent life. We also tried to see what the impact was of the time between patent application and IND filing. Both of those things had an impact on effective patent life. The regulatory period had a small impact; the other period had a substantially larger impact.

Mr. **Walker**. The point being that if the company is slow in filing, they lose that time under the bill anyhow; is that not correct?

Ms. **Valtri**. That is absolutely correct.

Mr. **Gore**. Would the gentleman yield?

Mr. **Walker**. Yes.

Mr. **Gore**. The time period between the filing of the patent application and the issuance of the patent application is also partly influenced by decisions made within the company. Now, what I would like to ask of Mr. Balmer, is that not the case?

Mr. **Balmer**. Well, yes. There certainly could be an influence from these decisions. It is hard to quantify how much of an effect that has in the overall process. If I understand your question correctly, and I think what you are trying to get at is can the companies delay the issuance of the patent since it issues later, they are further into the regulatory procedure, they have lost less of their patent term. Conceivably there is very much an opportunity to do that. Whether that is effectively used or not, we cannot testify to.

Mr. **Gore**. Do you know of instances where that has occurred?

Mr. **Balmer**. Personally I do not know of any instances. The only information that we have developed specifically on that was contained in the letter which we sent to Mr. Walker yesterday, which indicated some of the histories of the patents involved with these 12 drugs.

In keeping with the traditions started earlier in the proceeding, maybe we should identify the source of the chart. Was it GAO——

Mr. **Clement**. It was made up by the staff of the industry.

Mr. **Gore**. Pharmaceutical Manufacturers Association?

Mr. **Clement**. No, the industry, Mr. Chairman.

Mr. **Gore**. Let us take the example of Spectrobid. Do you have the specifics of the patent filing there?

Mr. **Balmer**. Yes, I do, Mr. Chairman.

Mr. **Gore**. The first patent was filed September 7, 1971?

Mr. **Balmer**. That is correct.

Mr. **Gore**. Were there any intervening actions by the company before the issuance of the patent on March 26, 1975?

Mr. **Walker**. If I could just ask one question. Is this coming out of my time? You had asked me to yield.

Mr. **Gore**. The Chair will not penalize the gentleman.

Are there any intervening actions by the company at the Patent Office?

Mr. **Balmer**. In the U.S. Patent Office there are no intervening actions of the patent or the compound issued some 4½ years later, March 25, 1975.

Mr. **Gore**. Is there any indication from the record of that drug what the cause of the delay at the Patent Office might be?

Mr. **Balmer**. We have not investigated the records.

Mr. **Gore**. What about Ludiomil? They filed November 9, 1961, issued the patent 7 years later. Were there any actions by the company?

Mr. **Balmer**. Our records indicate that Ciba originally filed a patent on the drug in Switzerland the end of November 1960. Under convention they filed within 1 year in the United States, which is the date you gave. On October 19, 1964, they filed a continuation-in-part application.

Mr. **Gore**. A continuation-in-part application?

Mr. **Balmer**. That means that the application which they had originally filed was refiled and encompassed more subject matter, included some new information.

Mr. **Gore**. I see. You are familiar with these other drugs. Were there similar continuation-in-part applications for any of these others? I do not want you to address specifics——

Mr. **Balmer**. Yes, sir, there were.

Mr. **Gore**. Were there subsequent applications after the initial application?

Mr. **Balmer**. That is true, sir.

Mr. **Gore**. And one might conclude that a company which has an interest in extending the time of the—the time that the clock starts running on the patent has an opportunity to do so. I will not ask you to comment on that. We are going to have to move on.

Mr. **Walker**. I would like to point out that in the case of the drug that he mentions, we talk about average time for patents of I think he was talking about Ludiomil. The average life of patents is, from application to the issuance of the patent is 2 years. In that case it was 3 years before the continuance was requested. So that there is a time frame there. You know, all of this does not have any meaning, because all the things we are talking about in that period of time comes out of the company's hide anyhow if 1937 is passed. The reason I keep coming back to that is the fact that one of the purposes of this hearing evidently is to get a delay in consideration of 1937. What I am saying is that it seems to me, and this is what I would like you to confirm, that the data that you have come up with here really relates to other factors in the process rather than the process as detailed in 1937, and that is whether or not the regulatory time should come out of the company's hide or not; is that not correct?

Ms. **Valtri**. It looks at the causal factors for effective patent life.

Mr. WALKER. Insofar as regulatory period, your figures basically confirm what the figures are on that chart, the difference between 7.4 years and 13.1 years, is that not correct? On an average?

Ms. VALTRI. I did no analysis on your last column there, so I cannot completely answer yes.

Mr. GORE. Does the 7.4 years include all patents, or just the initial patent?

Mr. WALKER. It is new drug approvals of 1980.

Mr. GORE. But does it include the effective patent life of all subsequent patents, or does that just measure the running of the clock from the initial patent? To take the example of Ludiomil, does the continuation-in-part filing later on get reflected in that figure? I do not think it does.

Mr. WALKER. Reflected in these figures are the product patent.

Mr. GORE. The initial one or including the subsequent ones?

Mr. WALKER. The initial one.

Mr. GORE. So if a subsequent patent extends the effective patent life in the exclusive marketing period of the company, then that is not reflected in these PMA figures?

Mr. WALKER. I assume that the gentleman is referring to the process patents, and really I think that that does not really enter in here, because I do not think that we can come up with any drugs where the patenting of the process affects the end product of the drug. So that the patenting of the process really does not affect the product, and so what we are referring to here is the product itself.

Mr. GORE. If the gentleman will yield, and we do have to get to Dr. Hayes. The central assumption on which this legislation is based is that Government regulation is the principal cause of the decline in effective patent life for drugs in this country. If the decline in effective patent life is due more to decisions made by the companies than to factors within the control of the companies, then that central assumption on which the legislation is based is gone. Now, in a very quiet and impartial way, the analysis performed by the OTA staff has demolished the principal assumption on which the legislation has been based.

Now, there are other assumptions on which it is based and other reasons for which one might choose to support the legislation that is proposed. But if one——

Mr. WALKER. If I may reclaim my time, I think it does nothing of the kind. It does not demolish it at all. In fact, we have testimony that the study done by OTA confirms the point that there is a period of time in the process that the regulatory process takes away from the effective patent life, and therefore that the need for the legislation remains, that there is a need to take out of the patent process that amount of time which the Government is taking away from the lifetime that the company has on the patent of the drug.

Mr. VOLKMER. Would the gentleman yield? I have been a little disturbed about some statements that have been made here by the OTA people. I would like for them to send me in writing a further analysis. I have noticed here that the time—we will compare the time between the application patent file and the IND received or filing. That is one time period which you say is important. Now let us take the time period between the IND received and the NDA approval. And let us look and see on the same ones excluding, if you wish, the Meclan one, because we all admit that that is no time period there because it never was brought up before the time period expired.

But let us take the rest of them, all the rest of them. And we find that more time is elapsed between the period that it was in the regulatory process than the time elapsed between the IND or the patent application and the IND filing if you give each company 2 years, give them 2 years to do it. I think we have to give them some time to make their studies and their tests. You take those 2 years, you find that the regulatory process is a lot longer than the other, and yet you say the other is more significant than the regulatory process.

Let us look at Cinobac, the time period in regulatory process is 8. The time period between application for patent and IND received is 1 year. Meclomen, 15 years in the regulatory process, and only 2 years lost on the other end. But you say it is significant. I think 15 is a lot more than 2. If you take Vansil, 10 years in the regulatory process, no years in the filing. If you take Calderol, 7 years in the regulatory process, 2 years in the filing. If you take Yutopar, 9 years in the regulatory process, 4 years in the filing. Asendin, 11 years in the process, 3 years in the filing. Zomax, 6 years in the regulatory process, and 5 years in the other, in the filing. Siseptin is 7 years in the regulatory process, and it is 3 years in the filing. Ludiomil, 11 years in the process, and 5 years in the filing. Spectrobid, 4 years in the process, and 3 years in the filing. Now, if the process is longer than the filing period delay, how can the filing period delay be more significant than the regulatory process?

Mr. GORE. I presume the gentleman is asking——

Mr. VOLKMER. I would like a written answer on that. That is what you said.

Mr. GORE. I am sure they will be happy to provide that.

Mr. VOLKMER. You have said that here today.

Mr. GORE. The gentleman's time has expired.

Mr. WALKER. I thank the chairman for his indulgence.

Mr. GORE. I would like to thank our witnesses and the central point of the analysis in the record remains that statistically the relationship between the Government regulatory period and the effective patent life were drugs approved in 1980—the only year for which we have been provided data—is an insignificant one.

With that, I would like to thank you all for your work and your testimony.

Mr. GORE. I would like to call our next witness, Dr. Arthur Hull Hayes, Commissioner of the Food and Drug Administration, accompanied by Mr. Robert Helms, Deputy Assistant Secretary for Planning and Evaluation for Health.

Gentlemen, we appreciate your patience. Please come up to the witness table.

[Witnesses sworn.]

Mr. WALKER. Mr. Chairman, since I have to leave in a couple of minutes, I would like to take the opportunity to welcome Dr. Hayes to his appearance before this subcommittee. He is a distinguished son of the Pennsylvania Dutch country. I certainly would like to welcome him this afternoon.

Mr. GORE. I would like to welcome you too, Dr. Hayes, and say for the record what a joy it has been to work with you since you have taken over the FDA.

We have had some differences of opinion on several issues, but I think that you are a real standout in the new administration. I appreciate the work that you are doing and the cooperative relationship that we have had.

Without objection, the entire text of your statement will be included. We would invite you to proceed as you see fit.

If you care to summarize, that is all right with us.

STATEMENT OF DR. ARTHUR HULL HAYES, JR., COMMISSIONER, FOOD AND DRUG ADMINISTRATION, ACCOMPANIED BY ROBERT HELMS, DEPUTY ASSISTANT SECRETARY FOR PLANNING AND EVALUATION/HEALTH AND TOM SCARLETT, GENERAL COUNSEL

Dr. HAYES. It is a brief statement. There are highlights I would like to read if I may, Mr. Chairman.

I am pleased to be here today to discuss patent life and pharmaceutical innovation with you. I view this issue as a very important one and I wholeheartedly agree that there is a need for a careful examination of it. Accompanying me today is Robert B. Helms, Deputy Assistant Secretary for Planning and Evaluation (Health) and to my left Mr. Tom Scarlett, the Chief Counsel for the Food and Drug Administration.

In the pharmaceutical industry, high development costs and risk of failure are standard and small potential markets are not uncommon. As an additional disincentive, innovators of new drugs, medical devices and other health-related products typically lose years of patent exclusivity because of testing and regulatory review. Consequently, the Department has expressed support for patent life extension legislation, now pending in the Congress, as a means of encouraging innovative pharmaceutical research.

We should keep in mind, of course, that an exclusive marketing period is just one of the variables that manufacturers consider when deciding to invest in product development. Drug firms and other sponsors must carefully weigh a host of complex and interrelated long-range factors such as inflation, interest rates, availability of capital, scientific resources, response of competitors, changing technology, patient population, and regulatory review before deciding whether to start down the long trail of drug or device development.

As you can understand, most of these factors are ones I cannot influence. For those within my control, I have taken a series of steps to encourage invention and research. For example, we are working to reduce the premarket approval process time by revising the new drug regulations and through the efforts of a 21-member Task Force (for the Review and Improvement of the Drug Approval Process) which I appointed.

We have received many suggestions for improvement and are looking forward to receiving the recommendations of the Commission on the Federal Drug Approval Process sponsored by you and Representative James H. Scheuer. Also, as part of the Department's regulatory relief initiative, I am chairing a task force to review ways to streamline the investigational new drug/new drug application processes in order to reduce the time required for new drug development and review. In addition, the Department is conducting a management study of the paperwork flow and decisionmaking process for new drug applications. Regardless of the outcome of these efforts, however, our premarket approval system must continue to be thorough enough to assure the safety and efficacy of new drugs, even if that means living with a process that takes longer than we would ideally prefer. We can encourage innovation, but not at the expense of safety.

A number of trends should be taken into account in determining the effect of patent life on innovation. One trend is the increase in the time required to develop a new drug. During the late sixtys and early seventys, the average time from the request to perform clinical trials on humans to the submission of the new drug application was about 3 years.

Today it has risen to 5 years. Coupled with the average time of 2 years for the review of the new drug application and for the firm to correct any deficiencies found in the review, this means that the average new molecular entity entering the market today has been under development for 8 to 11 years—7 years under regulatory review plus the 1 to 3 years that occurred before the request to conduct human trials was submitted.

An additional trend affecting innovation is the rising estimated cost of drug development. We at the FDA are not in the best position to judge the accuracy of the various estimates which have been given, but we know that since 1960, the cost of discovering and testing a new chemical entity has risen faster than the rate of inflation. Various economic analyses taken together suggest that the present value of research and development costs for the successful introduction of a new drug ranges from $54 million to over $70 million. It should be kept in mind that these figures include the cost of initial research, in which companies "look around," so to speak, for promising developments, and also include the costs of the company's failures.

About 90 percent of chemicals which are investigated for potential marketing fail in the investigational phase or before new drug approval is sought.

For those that succeed, we have seen estimates that firms need an average product life of 12 to 19 years to cover the costs of research and development and earn a rate of return on investment equal to 8 to 10 percent per year. If only 6 to 9 years of proprietary marketing remain for the typical drug firm by the end of the regulatory review period, there is less chance that the firm can expect to receive an adequate return on its investments. This shortfall adds an additional element of risk that an innovator must consider when deciding whether to go forward with development. Although the degree of risk will vary depending on the particular product and market, the innovator's ability to assess the risk is often complicated by time spans that can cover a decade. Patent restoration would alleviate at least some of this uncertainty and a portion of the risk.

I also expect that patent restoration would help the smaller research and development-oriented companies because it would help them find investor capital on a competitive basis. The small firms often are forced to abandon the development of new products because of the extensive cost. It is to be hoped that the assurance of increased patent protection and the expectation of revenues should help these companies to start new projects and complete the development of existing ones.

In this regard, I am convinced that a healthy amount of innovative work from as many sources as possible is the best insurance against a monopolistic market in the drug and device industries. It is already common in some areas of these industries for improved designs and products to leapfrog ahead of products that have been available for relatively short periods. The work going on in the area of heart pacemakers is a good example. Patent restoration would help protect against monopoly rather than foster it.

The extensive evolution in science and medicine of the last few decades has enormously increased the complexity of drug and device development. New drug and device development in the future is going to to be an even more technically complex and expensive process, and will require more long-term planning and investment by the industry and others who sponsor new drugs and devices in this country.

There are already numerous examples of landmark new drugs or processes such as calcium blockers, hybridoma, or recombinant DNA that require a decade or more to develop and test before they can be safely marketed. In this era of rapid technological evolution, moreover, drug developers must also project well beyond the original process or drug product while it is still being developed, and anticipate probable changes that can result in second and third generation products.

As an example of foresight in research, a single "third generation" cephalosporin can now provide antibacterial coverage for an incredibly wide range of infections, including many which can be life-threatening. This nontoxic drug represents a marked advance over the second generation cephalosporin, which itself provided broad coverage. All totaled, it took over 10 years to reach the third generation stage.

The complexity of the technology required for these products was formidable. Sizable investments in facilities, staff, and equipment were required by those who could and would gamble millions of research and development dollars.

I recently announced FDA approval of a new vaccine for hepatitis B, a debilitating liver disease which is a major health problem in the United States and an even greater problem worldwide. Recent research on the hepatitis B virus has suggested an association with liver cancer, the most common form of cancer in the world today. Patients with liver cancer are more likely to have had chronic infection with hepatitis B than the general population. This vaccine may save people not only from an infectious disease, but from one form of cancer as well. Unfortunately, the new vaccine is terribly expensive and only can be made in limited quantity.

But, if we could produce it with recombinant DNA technology on a scale sufficient for mass inoculation, the effect worldwide, quite frankly, might be breathtaking.

We may also be able to achieve significant results by exploiting the prostaglandins, which are substances found in every cell of the body and which affect a large number of body processes. We do not yet understand everything that they do, but now that we know how to synthesize them, our ability to affect prostaglandin levels in the body may have beneficial effects in many areas. Only two prostaglandin drugs have been marketed so far, one for induction of labor and the other for the temporary maintenance of a particular congenital defect until surgery can be performed.

I am also optimistic that sustained release preparations exemplify a new technology that will lead to significant results. Sustained-release preparations have already been approved for the treatment of glaucoma and motion sickness. I hope in fact that these represent only a beginning.

As the history of almost every drug has shown, such improvements in medical science are not likely to take place without the investment of substantial private resources to find the answers.

I am mindful of the potential irony that, by performing careful and effective science, the Food and Drug Administration may be contributing to a decline in innovation in the pharmaceutical industry. Streamlining our regulatory process will help, but it can only go so far without adversely affecting the practice of good science.

Broadly speaking, we know that if we convert one of the constraints in the business environment to an opportunity, we will improve the businessman's expectations about the future. And, while I am aware that there are pitfalls associated with predicting exactly how business will react to a proposed change in government policy, I do think that any reasonable step we can take to put the pharmaceutical business in a better position to intensify its research and development activities is extremely important. In our view, patent restoration is such a reasonable step.

Mr. Chairman, this ends my formal statement. My colleagues and I will be happy to answer any questions you may have.

Mr. GORE. Thank you very much, Dr. Hayes. I take it your colleagues don't have prepared statements?

Dr. HAYES. They do not.

Mr. GORE. Mr. Volkmer?

Mr. VOLKMER. Do I understand you support the legislation for patent restoration?

Dr. HAYES. I do, sir.

Mr. VOLKMER. Do you believe then that it will lead to further continuing development of new drugs than if we don't have it?

Dr. HAYES. That is my fervent wish and the reason I am in favor of the legislation.

Mr. VOLKMER. And that it will also impact, of course, a lot on some of your smaller research-oriented companies?

Dr. HAYES. I believe it will.

Mr. VOLKMER. How long have you had experience or studied the problem? Can you tell us?

Dr. HAYES. You mean the particular problem of patent extension or of drug development?

Mr. VOLKMER. Drug development.

Dr. HAYES. I have been doing it myself as a physician and clinical investigator for some 15 years. I have only been involved for 10 months as Commissioner of the Food and Drug Administration.

Mr. VOLKMER. You have had in the past experience in drug development.

Dr. HAYES. I have indeed.

Mr. VOLKMER. Can you tell us from that experience whether or not the motivation for research has been contributed to by the possibility of profits in the future?

Dr. HAYES. My own experience does not tell me that. I was not involved in the pharmaceutical aspect but rather in the clinical testing. It seems reasonable that because the drugs we are testing today and the devices being developed today are more complex, the ways for testing and monitoring them ever more complex and very much more expensive in terms of time, facilities, equipment, and the like, the money must be there to pay for it.

Mr. VOLKMER. R. & D. costs more.

Dr. HAYES. No question about it, sir.

Mr. VOLKMER. Those costs have to come from profits then?

Dr. HAYES. They certainly have to come from those developing the drugs. The clinical investigators do not have the funds or the facilities.

Mr. VOLKMER. My point is, if you have no money to do the R. & D. with, there is no R. & D.?

Dr. HAYES. That is correct, sir.

Mr. VOLKMER. There would be no further innovation, no further drugs?

Dr. HAYES. That would be the end result if it all stops, that is correct.

Mr. VOLKMER. In other words, let's turn it around from what previous witnesses testified. I meant to ask them this question and didn't. What if we didn't have a patent on drugs? Let's say we didn't have any patent life at all.

As soon as you filed for FDA approval and the FDA approved it, everybody could come in and start taking up the formula and start manufacturing. How much research and development would we have?

Dr. HAYES. I am afraid I can't predict that, sir, because it is so different from the system we have.

Mr. VOLKMER. Do you think there would be very much of it? Would you go to the expense of $33 million knowing that the guy next door could open up and manufacture the same drug as soon as you did?

Dr. HAYES. Even though I have never been in the position of having $33 million at one time, I must say I think I would have second thoughts.

Mr. VOLKMER. I think most firms would. What I am afraid of is, at the same time as the patent life, which protects the formula, is decreased, the motivation for further research and development is also decreased?

Dr. HAYES. That certainly seems logical. Though I am not an economist in this area, and I do not think there are figures that allow an absolute prediction of what will happen, given certain changes, greater recouping of money or the like, there is no question that the complexity of the drugs and devices and the expense of the research necessary by 1982 standards, and beyond, to show that drugs are safe and effective; that devices are safe and effective; that those costs can only increase; that the excitement in innovative research, ways of producing drugs, drugs for new cases, drugs with very special problems in terms of their development and testing; that all of these are expensive; and if we are to see a continuation and indeed a growth in exciting new forms of therapy and especially in preventive medicine, then there is going to have to be a significant investment.

It is not possible to develop recombinant DNA technologies, new cardiac drugs, test them adequately—retesting criteria increase as signs and expectations increase—without a significant investment. Somebody has to pay for it. I think those who are making the long range decisions 5, 10, 15, 20 years in advance, have got to have some assurance they are going to have the money to do it.

Mr. VOLKMER. Thank you.

Thank you, Mr. Chairman.

Mr. GORE. Thank you.

Dr. Hayes, an increasing presence by FDA in the drug development process, an alleged increasing presence through lengthier regulatory requirements is cited by proponents of the patent term extension legislation as justification for the change.

Through my work with Congressman Scheuer in setting up this commission and with others, the Congress and the FDA together have had a continuing dialog to achieve a mutual goal of insuring that the drug approval process works as efficiently as possible.

Do you believe that we are making progress toward that goal?

Dr. HAYES. Oh, I think we are making very significant progress. I would like, if I may, Mr. Chairman, to point out one thing. The term this morning, "regulatory time," has been used in citing 7, 8, 9 years for various drugs from the time of the filing of the IND, that is requesting permission to first put a chemical substance or use a medical device in man, if it is appropriate, to the time that it is approved and on the market. That is all called regulatory time.

Only a small part of that, as I earlier suggested, is review time within the FDA.

Mr. GORE. Yes.

Dr. HAYES. That can take anywhere from 4 or 5 months to several years, depending upon the complexity of the drug, adequacy of documentation, and the like.

I think that perhaps a better marshaling of resources—some streamlining in terms of paper work or managerial expertise changes—can shorten that review time without diminishing the adequacy of the review with respect to efficacy and safety.

The longer period of time, but still lumped in this regulatory time, is the time spent on human testing. This time begins from the filing of the IND to the submission of the NDA; then the clock on FDA review time begins. That time, although it is obviously influenced by the Food and Drug Administration, is really influenced by the FDA only indirectly. It is influenced because of the law that requires safety and efficacy. It is influenced albeit through the FDA by the science today. What is it that it takes to prove that a particular drug is safe and effective in 1982 and are those requirements more stringent because of the science and the public expectations than they were 10 years ago?

So to say that the FDA can alter by fiat how long it takes to test a drug prior to the submission of the NDA is not true. The only way you could reduce that time to a vanishingly small amount would be either to turn back the hands of science and clinical medicine and what science and clinical medicine can do and expect to do or to repeal the safety and efficacy provisions and merely put any drug on the market that has been synthesized in a laboratory.

Mr. GORE. Most of the time that is designated as regulatory time is time during which the company is performing tests and finding things out about the drug in question and only a relatively short period of time is used by the FDA to review the work done by the company?

Dr. HAYES. That is correct. The proportion is larger. That is not to diminish the importance of efficiencies in the review time but it is not all homogenous time.

Mr. GORE. How much of that work that the company does would be done even if there was not an FDA in order to assure its customers in any subsequent lawsuits that the product it sold was, in fact, safe?

Dr. HAYES. If you are talking about safety, it is a difficult issue. We have had laws and regulations about safety for so long that I think it would be almost impossible to project what a company would do, how insurance underwriters would view a drug in terms of research. I do not think they would know what was safe unless they amassed their own science and minimultiple FDA's. I can tell you in terms of efficacy. Before the efficacy requirements were passed, while many drugs were shown to be effective by some manner of criteria, all were not, as the retrospective review in the DESI program clearly has demonstrated.

Mr. GORE. You certainly support the efficacy requirement?

Dr. HAYES. I think it is an expectation of the health professionals in this country.

Mr. GORE. Some experts have said that because of concerns about legal liability most all of the work done in testing drugs would probably be done today even if there was no regulatory agency. Do you have any reason to disagree with that, or is your testimony that you just don't have any evidence to make a statement?

Dr. HAYES. I do not think there are the data there to know what would happen in a situation which we have never had, at least not since 1938, with respect to safety. With respect to efficacy, I think there is a great deal of potential debate.

Mr. GORE. Your testimony further is that we have made progress and you have made progress in speeding up the review period, keeping in mind that that period is only a fraction of the total time now designated as regulatory time.

You have made progress in speeding that up. Do you expect further progress in the future?

Dr. **Hayes**. Oh, I think so. It will never be a time that is so short that it is inconsequential. In fact, it varies greatly, as was said in a different connection earlier today; means can sometimes be deceptive. You have to look at the range.

The time it takes to review a drug depends upon a number of factors: the number of patents, the type of drug, the complexity of the drug, the disease or diseases for which the drug was studied, the complexity of the monitoring or the data that comes forth, even the decision about efficacy with respect to safety and vice versa.

Clearly there are some drugs that may be very effective and also may have significant toxicity; but if there is nothing else that is effective at all, then it is a different sort of safety decision.

So there is a great variation. Indeed, the submissions to the FDA vary in quality, adequacy, format, and the like. So there is always going to be a range. I think it is good business, good management, as well as good scientific practice, to make an adequate review as efficient and as speedy as possible. It will never be zero. It will always be a significant time. I trust it will be shorter than it is today.

Mr. **Gore**. Patent term extension would not have a material effect on the speed with which drugs move through the review process at FDA, would it?

Dr. **Hayes**. I don't see how it would affect what we do. That is dependent upon where the science is today.

Mr. **Gore**. Any advances in the science at FDA would presumably also have a positive effect on the companies in their testing procedures?

Dr. **Hayes**. Well, I think the better the scientists are at the Food and Drug Administration, the more efficacious it is for the review process. But it is a two-edged sword.

As the science becomes more complex, as we more refine and make more complex our definition of a safe and effective antiarrhythmic or antimicrobial or the like, clearly this puts a certain burden on the amount of testing that has to be done to show it is safe.

We could show some drugs were safe by 1938 standards in a much shorter period of time with fewer patients or subjects than we can today. There is no way we can turn back either the public expectation or the scientific clock to 1938.

Mr. **Gore**. Do you think the FDA's new fast track for quickening the approval of new drugs with particular therapeutic programs play a major role, can play a major role in speeding up the process of approval?

Dr. **Hayes**. Oh, for those drugs I think there is no question about it. What you are really talking about is a marshaling of a finite amount of resources based upon a public health need.

Mr. **Gore**. So an important innovation that has great promise for the public health under the new procedures you established, it will come out much quicker from the FDA?

Dr. **Hayes**. Well, yes. I don't know how to define much. I think the track record is already clear that those drugs are approved more quickly, and I think the public health demands it and no one argues. It is always at the expense of something else. Without infinitely expandable resources, if you do some things faster, you obviously can't be doing other things as fast.

Mr. Gore. As I said at the beginning, I have enjoyed working with you in a mutual effort to try to speed that process up.

I am pleased we have made progress and that more can be expected.

Let me ask a couple of questions to Mr. Helms.

Secretary Schweiker also endorsed the concept of patent term extension for pharmaceuticals. He made the announcement at the same time that he announced reinstatement of the paper NDA policy, one that is designed to promote competition in the industry.

What are the implications for consumers in your opinion of the patent term extension?

Mr. Helms. I think it gets back to the basic question we are addressing today. I would agree with Commissioner Hayes and even the OTA testimony that there is no absolute way, using economics and emperical evidence, to say for sure that an extension of patent life will result in more innovation.

However, there is a good bit of historical evidence as well as theoretical models that indicate that it might happen, that we will actually get more innovation.

I think the implications for consumers are for more drugs to choose from. If we get this additional investment—as I have every reason to believe we will—consumers are going to gain from a larger supply of drugs. Consumers will have greater choice about the treatment of various kinds of diseases.

Mr. Gore. There is no assurance that innovation would be stimulated. You believe that it might be. What about prices? Do you think that the prices for prescription drugs would on an average increase, decrease, or remain the same?

Probably go up, wouldn't they?

Mr. Helms. Not necessarily. We know from studies of drug prices that there is great variation in how drugs are priced both before and after patent expiration. Some drugs hold their prices and market share, but the usual case is for both prices and market share to decline when a drug goes off patent. If we get more innovation, there is a good chance we may get greater competition within each therapeutic class. This may actually result in more price competition.

But it is conceivable that, if the patent life is extended, some particular products may have slightly higher prices. If companies are to be encouraged to engage in more R. & D., they are going to have to have the expectation of an increased cash flow in the future. Therefore, it is possible that consumers may pay slightly higher prices for certain products, although I would view this possibility as the exception.

Mr. Gore. I recognize Mr. Clement, minority counsel.

Mr. Clement. Thank you, Mr. Chairman.

Dr. Hayes, your background is as a clinical researcher?

Dr. Hayes. That is correct.

Mr. Clement. So you are very familiar with the safety and efficacy testing?

Dr. Hayes. I am.

Mr. CLEMENT. There has been an allusion that much of this safety and efficacy testing would be undertaken by the industry for legal considerations, for their eventual protection, for management decision purposes, or for societal purposes.

In fact, let me ask you, isn't full safety and efficacy testing of new drugs now required by public law?

Dr. HAYES. It is indeed.

Mr. CLEMENT. So manufacturers have no choice whatsoever? They must conduct full safety and efficacy testing?

Dr. HAYES. That is correct.

Mr. CLEMENT. That is required by the same government that issues the patent?

Dr. HAYES. Yes, sir. The U.S. Government.

Mr. CLEMENT. Let me ask you, what percentage of pharmaceutical R. & D. in this country is carried on by those companies that have been characterized as production intensive and what percentage by those that are characterized as research intensive?

Dr. HAYES. I am not sure that I can give you figures. It is really not my area. I am told that the funding of research and development for new drugs—probably some 80 or 90 percent—emanates from the research intensive firms.

But I don't want to swear to those figures. It depends on whether you are talking about the number of drugs, number of patients, or dollar value. Each would produce a different result. There is no question that the majority are so developed.

Mr. CLEMENT. How would you characterize the trend, Dr. Hayes, on the effective patent life on new drugs over the last 20 years in this country?

Dr. HAYES. How would I characterize the effect? I think there is no question it has gone down.

Mr. CLEMENT. Significantly?

Dr. HAYES. Well, I am not sure one can apply a statistically significant test except perhaps beginning and end. I think there is no question that it is a significant decline.

Mr. CLEMENT. How would you characterize the trend on a comparison of drugs that are submitted or filed with the IND and new drugs approved over the past 20 years?

Dr. HAYES. I don't understand what you mean by how would I characterize them.

Mr. CLEMENT. On total numbers, on a quanity basis, how does the trend appear on new drugs that are filed for an IND?

Dr. HAYES. I think it goes up and down, especially if you are talking about since 1962. If you look at the number of new chemical entities, or new molecular entities approved by the FDA, it has gone up and down.

In 1981 there was a rather large number we approved, 27. In the previous year it was 12. It has varied.

There are a number of factors responsible for that, including the kinds of drugs and what research was necessary to demonstrate efficacy and safety. Obviously more is required for some kinds of drugs than others.

The decisions were made literally 10 or 15 years ago by drug firms, and the drugs were in the pipeline, if you will, in clinical development. They came to the FDA and the approval occurred in a particular year. There are a number of factors.

I must confess I don't see any particular trend in the new drugs that we have approved over the last few years. But I don't make anything out of the fact that there is no clear trend because you are almost talking about oranges and apples when you talk about some of these drugs. All drugs are not the same.

Mr. GORE. Will counsel yield?

Mr. CLEMENT. Absolutely, Mr. Chairman.

Mr. GORE. I think that is pretty significant.

Since 1962 you don't see any decline in the number of new drugs approved?

Dr. HAYES. Oh, I think over the long haul that probably there has been a decline.

Mr. GORE. Now, since 1962 has there been a measurable pattern of decline in the number of new drugs approved at FDA?

Dr. HAYES. Counting every drug as a single unit, then I am not sure there is an absolute trend.

Mr. GORE. The answer is no? There hasn't been?

Dr. HAYES. In terms of actual numbers, that is correct.

In terms of significance of the drugs, as I suggested, they are not homogenous, and I think as a pharmacologist and as a physician, I would be concerned about some of the developments. That is arguable scientifically.

Mr. GORE. Is it your testimony there has been a decline in the number of significant drugs approved?

Dr. HAYES. In some areas, I think so.

Mr. GORE. Overall? OTA testified there hasn't been.

Dr. HAYES. Of significant drugs. I don't know on what medical basis they make that decision. I think in some areas there has been a decline in significant drugs.

Mr. GORE. In some areas there has been an increase?

Dr. HAYES. That is correct.

Mr. GORE. Overall there is no perceivable pattern of decline?

Dr. HAYES. And in numbers none. That is correct.

Mr. GORE. Thank you.

Mr. CLEMENT. My final question, Mr. Chairman is, Dr. Hayes, based on your background and current position, you personally would support current legislation?

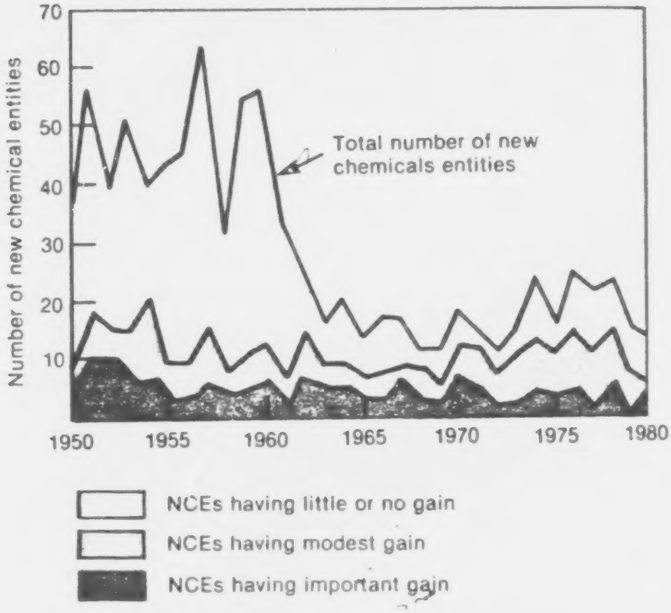
Dr. HAYES. I would in the hope and indeed in the belief that it will encourage innovation of new drugs. That is what I am interested in as commissioner and as a physician.

Mr. CLEMENT. No further questions, Mr. Chairman.

Mr. GORE. I would refer for the record—and without objection I would like to put it in the record—the chart developed from the testimony of Richard Crout before the Subcommittee on Health and the Environment of the House Energy and Commerce Committee. It is on page 26 of the OTA report.

[The information follows:]

Figure 2.—Annual Approvals of New Chemical Entities Reflecting FDA's Judgment of Therapeutic Potential



SOURCE: Testimony of J. Richard Crout before the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce. April 1, 1981.

Mr. GORE. It shows the number of new chemical entities having little or no gain, having modest gain, and having important gain. In fact, there is no pattern of decline for any of the three categories, particularly when you factor in 1981 this chart that stops in 1980. There is just no pattern of decline.

I would like to—I guess we better move on. I would like to thank you for coming here, Dr. Hayes. I would like to thank your colleagues, Mr. Helms and Mr. Scarlett, too. I appreciate your help. Thank you very much.

Our next witness is Dr. William Wardell of the Center for the Study of Drug Development, School of Medicine and Dentistry, Rochester University.

[Witness sworn.]

Mr. GORE. Without objection, Dr. Wardell, we will include the full text of your prepared statement in the record at this point.

We would like to ask you to summarize, since we are running late, if that is agreeable with you.

Let me tell you at the outset that it is the intention of the subcommittee to have a lunch break today out of courtesy to the members and the people who have come to join us today.

We will try to get through your prepared statement by 1:15 p.m., if you can help us in that regard, and then we will take a lunch break and come back for questions.

If you don't feel that that is adequate time for you, we will break at 1:15 p.m. anyway and come back and let you complete it.

Please proceed.

STATEMENT OF DR. WILLIAM WARDELL, CENTER FOR THE STUDY OF DRUG DEVELOPMENT, SCHOOL OF MEDICINE AND DENTISTRY, ROCHESTER UNIVERSITY, ROCHESTER, N.Y.

Dr. **Wardell**. Thank you very much, Mr. Chairman.

Before I start, I would like to check that you have the full submission that I made yesterday, the four appendices with appendix D being the data plus a computer listing of the 6 years of data.

Mr. **Gore**. Without objection, that material will be put in the record in full at this point.

Dr. **Wardell**. I would just like to check you have it. I would like to refer to it in some detail.

Mr. **Gore**. Is it in the orange folder here?

Dr. **Wardell**. Appendix D has it, but I would like you to have the computer listing as well. It is easier to read.

Mr. **Gore**. Yes, I have it.

Dr. **Wardell**. I am William Wardell from the University of Rochester Medical Center. I am also director of the University's Center for the Study of Drug Development.

I am very pleased to be invited to these important hearings because I believe that you and the other members of the subcommittee are looking into an issue of major national importance.

I believe the whole process of research and development in the U.S. high-technology industries has a critical impact on the Nation's economy and that these innovations will benefit people around the world while contributing favorably to our balance of trade.

I would like to start by taking a few moments to inform you about the Center for the Study of Drug Development and to make some general observations about pharmaceutical innovation here and abroad.

Our center was established about 6 years ago to study the process of pharmaceutical innovation. To our knowledge, it is the only one of its sort in the world that studies these particular issues.

Dr. Louis Lasagna is the chairman and I am the director. This, incidentally, is not our only job. We are full-time faculty members of the University of Rochester Medical Center and our responsibilities are to teach, to do research, to see patients.

This is not the only research we do. Both of us have skills in clinical pharmacology and I do drug studies as well. I also have a lab but I don't have much opportunity to get to it these days. I think of all the work we do, the research on pharmaceutical innovation through the center is probably the most prominent.

We deal primarily with the scientific and medical aspects of the drug development and regulatory process and also with related topics such as surgery, medical devices, patents, and even economics when we collaborate with professional colleagues.

During the past 6 years, the center has amassed very large data bases for studying the drug development process in the United States. I concentrated on this when I set it up because when we began there wasn't much information on this. So we concentrated on two sorts of data. One, published materials. We have a library of about 9,000 or 10,000 items, computer sorted, and this is a major resource for research and for teaching.

The other sort of data base is data on drugs, and I took particular pains to make this very comprehensive.

In the data base of public data, we have records on all drugs marketed in the United States since about 1940, going back to where they came from, how they got started, when they went through the various stages of the process.

We also have a data base of mainly proprietary information on all drugs that entered research in the United States since the IND requirement in 1963, and even before that. Because the success rate from the filing of the IND to approval for market is about 9 or 10 percent, this is about 10 times the size of the marketed-drug data base.

Patents were one piece of information we began picking up about 5 or 6 years ago and have developed in terms of the factual data base continuously since then.

We have about eight staff, including three postdoctoral fellows and we support research activities; that is, we provide facilities for other people in the university and abroad.

We get quite a lot of visits. The People's Republic of China sent us a delegation of eight people once to see how we did things; also the Italian Government, and the Japanese pharmaceutical manufacturers.

At its formal opening, the center's chairman, Dr. Louis Lasagna, set out its purpose as follows:

> The Center for the Study of Drug Development will devote its energies to the exploration of the problems that keep drug development from being optimally beneficial to the public. A basic objective is to study the entire process of how drugs are discovered, evaluated, developed and used. Important considerations are the points where science and public policy come together, including regulation and economics. On the whole, basic research has been of special interest to the academic community, while development has been the job of industry. Our Center hopes to bring these two sectors and government together. Government is particularly crucial because of the way drugs are regulated, and the effects of that regulation on the process of discovery and development. We hope to provide significant public service and to display the kind of scholarship to be expected from a center based at a first-rate university.

As I looked back at this statement in preparing for this meeting today, one of the things that I think we can claim to have done is to raise the factual standard of debate.

Looking back at the early days, I am impressed by how much debate there was, usually between government and industry, based on only very small amounts of data.

Now that I see the standard has been raised quite a lot, I take some pride in having contributed to raising that because, if one group has more data, the other group has to have better data in order to prevail.

Dr. Lasagna's words remain for our center a statement of our purposes and our aspirations. Support for our center is derived from government, from industry, and from foundations and from general university revenues.

A part of the center's work at present involves evaluating the factors that affect national R. & D. output and performance. There are only half a dozen or so countries in the world that develop new drugs in substantial numbers, and we have a number of projects at present that compare the performance and research output of the United States to that of Japan and the drug developing countries of Western Europe.

The European studies are supported by the National Science Foundation. At present I am just looking at Japan because I think that will be very important in the future. We are making exploratory examinations of Japan's pharmaceutical innovation.

One aspect of particular interest at present is how the governments of advanced countries foster the process of new drug discovery and how they regulate drug development.

I think one country can learn quite a bit from the others.

I would just like to mention a few studies that we have been doing for some time because they form the larger research environment that gave rise to our patent study which was a relatively small study in the context of our——

Mr. GORE. Where are you in your statement, Dr. Wardell?

Dr. WARDELL. I am at the top of page 3, Mr. Chairman. One-third of the way down.

At the outset, I would like to point out that ours is the only research group that has studied in depth pharmaceutical innovation through looking at new chemical entities or NCE's from the point where they enter the clinical stage of development. These studies have contributed substantially to the understanding of this important subject .

The beginning of clinical trials is really a key step in pharmaceutical innovation and the drug development process.

In fact, our first relationship with the National Science Foundation came when they came to me in 1974 and, having seen a study we did, which was the first one on new chemical entities on research in the United States, asked us to expand it to the whole industry so they could get a handle on what is happening.

Mr. GORE. Dr. Wardell, if you tell us an anecdote between each sentence, we are not going to get through the testimony. You know, we appreciate the work that you have done in this area, and I appreciate the opportunity to hear all about your center and we will include all of this material about the center in the record and we would like you to proceed with the issue at hand, if that is possible.

Dr. WARDELL. Certainly, Mr. Chairman.

Perhaps the one study that I would like to show you before I get to the patent life study, is one that looks at the rise in the time required to develop a new drug. I would like to show the first slide here.

Could we perhaps darken that end of the room?

Mr. GORE. OK. We are going to have to break for lunch. Maybe we will come back and pick it up here, OK?

We will break for lunch and we will come back at 2 o'clock and ask you to expedite the rest of your statement.

Then we will have questions and go to the rest of the hearing.

AFTERNOON SESSION

Mr. **Gore**. The subcommittee will come back to order.

My apologies to the witnesses and others. The Speaker was delayed by the arrival of the President of Egypt, Mr. Mubarek, and that is the cause for the delay.

We would like to proceed with your presentation, Dr. Wardell. I believe you were just about to get to the slides. Proceed as you see fit.

Dr. **Wardell**. I think because of the time factor I would like to go straight to page 8 and begin to answer your first question, and this is the one that I have the most detail on.

The first question is effective patent life: What factors should be taken into account in determining effective patent life?

I believe I can best answer this question by describing how we did our study and by discussing possible alternative approaches. We performed our study in 1979 and 1980 when there was a heightened general interest in patents stemming from the Carter administration's domestic policy review, which features patents in that main report, and specifically mentions pharmaceutical patents. As a result of your asking me to participate in these hearings, I have carefully reexamined both the data and the assumptions we used in that study, and have updated the information through the end of 1981. In fact, the data I have with me are our best as of last Friday, January 29.

I have confirmed that the data are accurate and the assumptions we used in analyzing them are very reasonable. Indeed, I think they are a little cautious, in that the average effective patent life of new drugs is even less than our paper showed. The results of our study showed that between 1968 and 1979, the effective patent life declined from 13½ years to 9½ years.

We found that three factors contributed to this 4-year decline. The most important was an increase in the time from the start of clinical investigation to the approval of the NDA. Most of that increase was caused by the increase of the IND time, since the NDA review time remained approximately constant. And that accounted for 60 percent of the decline in patent life. The second factor was the increase in the time from filing of the patent to the beginning of clinical investigation, and that has a bearing on what was discussed this morning on the OTA report. And the remaining 27 percent was due to a decline in the patent pendency period.

Point 1 deals with the data to be used in calculating effective patent life, beginning with the lists of drugs. You have to start by deciding what drugs are you considering. What is the study about, and how do you select the drugs? We focused primarily on new molecules, new chemical entities, because we are interested in pharmaceutical innovation, and we look at them as they are approved for the first time for human therapy in the United States.

The FDA's lists of NDA approvals are the starting point for this study. Note that most of the drugs on those lists are not NCE's, so they do not qualify for our analysis. In recent years, FDA has classified the new chemical entities, and its class 1 drugs come close to satisfying our inclusion criteria, but you do need to look at each drug individually. You need to keep the study focused on new chemical entities if that is the point of the study.

We excluded, for example, foods, diagnostic agents, vaccines, surgical sutures, contact lenses, devices, and new salts, esters, or combinations of molecules that have already been approved. We also excluded disinfectants, things used in dandruff shampoos, that sort of thing. In most cases there was no problem in determining which NDA approvals for NCE's to include, because it was obvious which are the new drugs, but there are from time to time a few drugs with special histories on which you have to use judgment.

Next, the drug development and patent data. The drug development data are quite straightforward. In this case it is NDA approval date, but for other things you might want the IND filing date. Next, the patent data. In designing our study, we gave much thought to which patents to include.

Mr. **Gore**. You did not include the IND filing date?

Dr. **Wardell**. We have all that.

Mr. **Gore**. It is not in the study and in the results?

Dr. **Wardell**. Excuse me, it is in the paper. I did not bring the IND data down today. This particular listing does not have it. Yes, it was required for the 1979–80 study.

We consulted patent experts, and because we were primarily interested in the original discovery of the new chemical entity, we went for the original compound patent, the chemical patent on the product. And we knew also that of the main sorts of patent, the compound patent is the one that provides the main protection and confers market exclusivity.

These assumptions of ours, I am glad to see, are confirmed by the OTA report and the statement of the Commissioner of Patents at the Kastenmeier hearings in November. Mr. Chairman, I am now at line 5 of page 11.

> Because the initial use and process for making the compound are generally disclosed in the compound patent, this information falls in the public domain on the expiration of the compound patent and can be used by anyone. In addition to the original process disclosure accompanying the compound patent, the ease of discovering alternate processes—together with the existence of foreign or concealed manufacturing processes in violation of existing process patents—serve to defeat market exclusivity as the result of process patents alone. In the case of use patents, it is possible for a new and different use to be patented for an existing compound, and such a use patent could outlast the original product patent with its disclosed use. However, such a use patent could only provide market exclusivity if the active ingredient had no other substantial use.
>
> In short, process and use patents normally do not provide any more useful information on EPL for the original discovery than does the compound patent. One should therefore generally use the compound patent where it exists.

These are the principles of the patent system that guided us in establishing the methodology for our study. And they are consistent with the OTA report and the statement of the Commissioner.

Now, drug data and patent data. Mr. Chairman, in appendix D, I have prepared in response to your request the list for the last 5 years, actually 6 years, right up through the end of 1981, and I would like to read the methodology statement, because that is an important description of how we went about finding the data and calculating the various means that are there.

The patent data refer to the compound patent where one exists: 85 percent of the drugs had compound patents. Where there was no compound patent, that is where there was never a compound patent, the earliest alternate patent was used.

The type of patent, date of issue, and patent number are shown against the drug name in these lists.

Method of calculating the mean effective patent life: The effective patent life of each drug is the time from NDA approval to expiration of the patent. Because there are several different types of patents, there is more than one value for mean EPL, so we used the following procedure to calculate a range of mean EPL values that reflect these different patents.

In the first set of calculations, if the drug was not patented or if the patent had expired prior to NDA approval, EPL was taken to be zero. If the patent was still pending as of January 1982, it was arbitrarily assumed to be a compound patent that will issue on December 31, 1982. There were one or two drugs in our previous study that had patents pending that have subsequently been approved. I think there is one in there that was pending previously and is still pending. So the pending ones are assumed to be issued on December 31 of this year.

An example of that is, for example, in 1981, the drug ketoconazole, which if it issued on December the 31, 1982, would have a patent life of 18.6 years. Mr. Chairman, note also that in this list the drugs are written by their nonproprietary or generic names, and there may be some translation needed to fit in with OTA's list, which are by brand name.

Results of the mean EPL calculations for each year are shown in the table underneath the list of drugs for that year. The means were calculated by the class of the patent listed, that is by the class of patent shown in the listing here, cumulated in the following order of patent type as shown under the heading "Patents Considered."

We took first the compound patent, then the compound or composition patent, then we added in the use patent, and then added in the process patent. Bear in mind this is not all such patents on each molecule, it is just the ones that are in the lists as defined above. The calculations were performed first with the denominator equal to the class size, "mean EPL of class," and then repeated with the denominator equal to all the drugs approved that year "mean EPL of year". So in the former case, that is the left-hand half of the table here, drugs lacking a relevant patent of this type are excluded, while in the latter case (the right-hand half of the table) we include such drugs but count them as having zero EPL. So in the latter case we get the mean, for example, of all the compound patents averaged over the drugs that had a compound patent plus those that did not have one, which are counted as zero.

In the first row of the left-hand side of the column, we show the mean of the compound patents where they exist. For 1981 there was hardly any difference between the left and right halves of the table, all have compound patents except for two drugs where this had expired before NDA approval. Where the definition changes (e.g. to compound or composition patent), the mean value can change in the results. Then if the original patent had expired before NDA approval, the next patent, where available was substituted; (the drugs that had a patent to substitute are shown in the remarks column); and these calculations were repeated. I should stress this is only where the first patent had expired by the time of NDA approval. These new mean values are shown in parentheses next to the corresponding unsubstituted mean values.

The above calculations were all repeated after excluding drugs that had no patents or for which the patent was expired or pending. This is labeled "Unexpired Patents Only," the one we used as the single value in the paper. It usually gave the most cautious value for EPL. Graphs of the average EPL values by year are shown in the last page of the appendix. The rest of that sentence is in the wrong place and should be deleted. That is the words "and summarized in table 1, see page 22."

The graph at the end of appendix D shows how the EPL value for unexpired patents only is generally the most conservative. That is, it shows the least erosion of patent life. So, as shown in these results, the above calculations give a range of EPL values that depend on which patents are considered. Considering the compound patents only and averaging over all drugs approved each year, the mean EPL for the years 1976 to 1981 ranged from 6.8 years to 8.5 years. If You add in the composition, use, and process patents shown in these lists, and substitute the next available patent for those that had expired prior to NDA approval, this increased the EPL range up to 7.1 to 10.8 years; but full protection is not necessarily conferred for the additional period. EPL based on unexpired patents only ranged from 7.3 to 11.4 years; that shows the cautious nature of our assumptions in the first paper.

There is a downward trend in EPL over the 6-year period. We see that in the graphs. The values for 1981 are the lowest that we have observed. In 1981 the average effective patent life for compound patents had declined to 6.8 years. And it is interesting, Mr. Chairman, to look at 1981, because there are only about seven drugs that have an effective compound patent life greater than 10 years, and note that six of those are drugs, four of them antibactuerial anti-infective. (One of the others is antifungal, the other is antimalarial.) If you remove the six drugs in the whole year that are anti-infectives, the mean EPL of the rest is 4.7 year. The anti-infectives themselves they have a mean EPL of 12.5 years—I was just doing this during the OTA presentation because there was some discussion about whether different sorts of drugs have different patent lives.

Getting back to the 6.8-year figure, I find this very remarkable. My conclusions are that the compound patent is not giving much protection for these compounds.

Mr. Chairman, would you like to ask any questions about the paper?

[The prepared statement of William M. Wardell follows:]

Statement of

William M. Wardell, M.D., Ph.D.

AT HEARINGS ON
PHARMACEUTICAL PATENT LIFE AND INNOVATION

Submitted to the Subcommittee on Investigations and Oversight
of the Committee on Science and Technology
United States House of Representatives

4 February 1982

I: INTRODUCTION AND GENERAL COMMENTS

I am William Wardell, Associate Professor of Pharmacology and Assistant Professor of Medicine at the University of Rochester Medical Center. I am also Director of the University's Center for the Study of Drug Development. Further biographical details are provided in the Appendix.

I am pleased to be invited to these important hearings. You, Mr. Chairman, and the other members of the Subcommittee on Investigations and Oversight, are looking into an issue of major national importance. The whole process of research and development in America's high technology innovative industries has a critical impact on our nation's economy, and our ability to assure that domestic needs are met. This nation's technological innovations ultimately benefit people around the world while contributing favorably to our balance of trade through successful international competition.

I would like to take a few moments to tell you about the Center for the Study of Drug Development and to make some general observations concerning pharmaceutical innovation here and abroad. I will then respond specifically to the questions posed by the Subcommittee in its invitation.

The Center was established about six years ago to study the process of pharmaceutical innovation. To our knowledge, it is the only university research unit in the world devoted to analysis of the whole process of drug development and regulation. It deals primarily with the scientific and medical aspects of the drug development and regulatory process, and also with related topics such as surgery, medical devices, patents, and economics. During the past six years the Center has amassed large data bases for studying the drug development process in the United States. These data bases are widely regarded as the most comprehensive of their type in existence.

At its formal opening the Center's chairman, Dr. Louis Lasagna, set out its purpose as follows:

> 'The Center for the Study of Drug Development will devote its energies to the exploration of the problems that keep drug development from being optimally beneficial to the public. A basic objective is to study the entire process of how drugs are discovered, evaluated, developed and used. Important considerations are the points where science and public policy come together, including regulation and economics. On the whole, basic research has been of special interest to the academic community, while development has been the job of industry. Our Center hopes to bring these two sectors, and government, together. Government is particularly crucial because of the way drugs are regulated, and the effects of that regulation on the process of discovery and development. We hope to provide significant public service and to display the kind of scholarship to be expected from a center based at a first-rate university.'

Dr. Lasagna's words remain, for the Center today, a statement both of our purposes and our aspirations. Support for the University Center is derived from government, from industry, and private foundations, and general University revenues.

Part of the Center's current work involves evaluating the technological status of the United States' total pharmaceutical research and development effort, in particular the factors that affect national research output and performance. There are only some half-dozen countries in the world which develop new drugs in substantial numbers. The Center has undertaken several projects that compare the performance and research output of the U.S. to that of Japan and the drug-developing countries of Western Europe. In this respect, one subject of particular interest at present is how the governments of technologically-advanced countries foster the process of new-drug discovery and regulate drug development.

The discussion today involves some of the core issues in pharmaceutical innovation. Several of the Center's studies--both published and in progress--deal with these same issues. At this point I will refer briefly to the main points of these relevant studies, but leave the specific details for my responses to the Subcommittee's questions.

At the outset I should point out that ours is the only research group which has studied pharmaceutical innovation by examining new chemical entities, or NCEs, from the point where they enter the clinical stage of drug development. We believe the resulting studies have contributed substantially to the understanding of this important subject. The initiation of clinical--i.e. human--trials of an NCE developed in the laboratory is a key step in pharmaceutical innovation. Thus, the number of NCEs entering human testing is an important measure of the extent of pharmaceutical innovation at an early stage. By tracing the progress of these NCEs through the clinical investigation and regulatory stages, we can identify factors which either encourage or impede the process of innovation. Our studies track the fate of all such compounds from first human testing to their abandonment or final marketing approval.

We have found that the time required to develop a new drug--i.e. from synthesis of the compound to approval of the U.S. NDA--has nearly doubled over the last decade-and-a-half. On average, this now takes over 12 years, of which approximately six years represent clinical studies and two years NDA review (See Table I and Appendix B7). Most of the synthesis-to-approval time elapses _after_ the patent has been issued. Therefore, unless some compensatory change has occurred in the patent process, the effective patent life will necessarily have diminished by a corresponding amount of time.

Certain of the measures used in our studies of NCEs do indeed show that pharmaceutical innovation in the U.S. is becoming more difficult and is declining, and that there is an increasing reliance by domestic pharmaceutical firms on foreign discoveries. This phenomenon is particularly striking in the case of the smaller U.S. firms. In the last few years, small research-based domestic firms have become nearly 50% dependent on licensed compounds for their clinical research programs. Overall, most licensed discoveries come from abroad.

Here in the United States there has recently been a steep decline in the number of new compounds (drug candidates) reaching the stage of human testing. It is not yet known whether this has been accompanied by a compensatory rise in the proportion ultimately approved for marketing (although some analyses we examined last month, and are still working on, suggest that a rise in the success rate may indeed be occurring).
But unless a radical and unprecedented rise occurs in the success rates of compounds already in research, we can expect that there will be a corresponding reduction in the numbers of U.S.-originated innovations reaching the market in the mid-1980s and beyond. The U.S. is probably not alone in this regard. Other drug developing nations, with the possible exception of Japan, seem to be encountering a shrinkage in the flow of new drug candidates.

The decline in pharmaceutical innovation warrants the high-level attention it has received because this is one of the main pathways by which the discoveries being made in biomedical research are translated into practical advances in medical therapy. Such innovation was responsible for the position of global preeminence in pharmaceuticals which the United States achieved after World War II. The slowing of pharmaceutical innovation may, as stated above, be an international phenomenon (again, with the possible exception of Japan), but the impact of the U.S. decline is of special global significance because of the large fraction of the world's biomedical research and pharmaceutical innovation accounted for by this nation. Obviously, too, it will affect the relative worldwide importance of this country in the field of pharmaceuticals.

The reasons for this decline in pharmaceutical innovation are complex and involve all parties to the innovative process--most notably industry and government. Underlying scientific determinants and economic constraints are also involved. But whatever the causes of decline, reestablishing this nation's innovative leadership in pharmaceuticals would unquestionably be facilitated by making the process of new drug development more efficient and by maintaining the incentives for research and development which have been so effective in the past.

Background of the Center's Patent Study

Our studies of NCEs, begun in 1975 under a grant initiated by the National Science Foundation and continued under our present NSF grant, have shown among other things a steady increase in the time required for the development of a successful drug. Most of the increase has occurred in the clinical phases, which in the U.S. are controlled by the IND regulations. These phases generally take place after the patent is issued. Therefore one would expect to see a corresponding reduction in the effective patent life (EPL) remaining after approval of the New Drug Application (NDA).

When we commenced our study it was already known that, since the mid-1960s, EPL had declined by approximately the same amount as the average increase in the clinical development time. In the absence of further details, we (and others) generally assumed that the one simply caused the other. In 1979, the results of the Carter Administration's Domestic Policy Review of Industrial Innovation became available, showing high-level concern about the state of innovation, and about the role of patents in the innovative process. Pharmaceutical patents were specifically mentioned in the Final Report of the Advisory Committee on Industrial Innovation.(C1)

In 1979 the Center already possessed a substantial amount of information on NCE patents. A corresponding amount of drug development data on every U.S.-approved NCE had been produced from our NSF studies. Some of these data had never been available before and were uniquely suited to analyzing questions involving the relationship between the drug development and the drug patent processes. It was then an obvious step to analyze, for each NCE, its passage through the patent process and to compare this with its passage through the drug development and regulatory processes. In this way we could find out where patent life was being eroded, and what factors if any (in addition to the increase in clinical development time) were contributing to this erosion. In the process we could also learn more details of general interest about the patent process and its relation to drug development--a fairly specialized subject on which there had been little previous work. Thus, although the patent study is a relatively small part of the overall project, it is nevertheless an important one.

The results of this study surprised us somewhat. Although the fall in patent life was (as expected) mainly accounted for by the rise in clinical (IND) development time, two other factors were also involved. We found an increase in the duration of the preclinical time and also a shortening of patent pendency (quicker issuance of the patent). In the course of this study we were also able to show details of the juxtaposition of the patent and drug development processes that had not been widely known or precisely documented before. See, for example, Figures 1, 2 and 3 of our paper.

I mentioned that Japan may be an exception to the general trend toward declining innovation. Recently, we have turned our attention to pharmaceutical innovation in Japan. While we have found a general trend toward declining innovation, it is my impression that Japan, of the half-dozen nations presently developing new drugs on a significant scale, may be the only one in which pharmaceutical innovation is *increasing*. I understand that there are certain regulatory policies which could increase Japan's national capacity for pharmaceutical research and development. These are in addition to longstanding policies that foster industrial innovation in general. The effects of all such policies bear close watching. If successful, they will obviously be of interest as possible models for U.S. efforts to maintain technological prominence.

It is also noteworthy that the U.S. is not the only country in which there are attempts being made to restore patent protection for pharmaceuticals. In the U.K., the pharmaceuticals sector working party of the U.K. National Economic Development Committee for the Chemical Industry has recently recommended that pharmaceutical patent life be restored by the time lost to compliance with regulatory requirements (up to a full patent life of 20 years). In Japan, the pharmaceutical industry is proposing to request that pharmaceutical patent life be extended from its present value of 15 years up to perhaps 20 years, because of the erosion of effective patent life.

II. RESPONSES TO SUBCOMMITTEE'S QUESTIONS

Mr. Chairman, I shall now address the four questions posed in your letter of October 1, 1981. For the most part we can respond to the questions with facts; however in one or two instances they involve matters of opinion on which I will give you my best judgment. Two of the attachments to which I shall refer are studies-in-progress that have not yet been published.(B6 and B7) While I do not expect the final results of these studies to be substantially different, they should nevertheless be regarded as preliminary.

(Question 1) Effective Patent Life: What factors should be taken into account in determining "effective patent life"?

I believe that I can best answer this question by describing how we performed the patent study I referred to earlier, and by discussing possible alternative approaches.

Our patent study(B1) was performed in 1979 and 1980, a time which coincided with a heightened general interest in patents stemming in large measure from the Carter Administration's Domestic Policy Review. In the last two months I have carefully re-examined both the data and the assumptions we used in that study, and have updated the information through the end of 1981. I have confirmed that our data are accurate and the assumptions we used in analyzing them are reasonable. Indeed, our assumptions are very cautious in that the average effective patent life (EPL) of new drugs is even less than our paper shows.

As indicated in Figure 2 of our paper,* the effective patent life of a newly approved drug is determined by two independent processes which proceed in parallel: the patent process and the drug development process. The main factors determining EPL are the time when the patent is issued, and the amount of time that clinical research and development and marketing approval consume after patent issue.

The results of our study showed that, between 1968 and 1979, the EPL declined from 13.5 years to 9.5 years. We found that three factors contributed to this 4-year decline: the increase in time from clinical testing to NDA approval, the increase in time from patent filing to clinical testing, and the decline in the patent pendency period. The absolute contribution of each of these varies somewhat from one year to another, but for the overall 1968-1979 period the lengthening of the time between the start of clinical testing and NDA approval--2.4 years--accounted for 60% of the total decline in EPL. By comparison, the time from patent application to the start of clinical testing increased by 0.5 years (accounting for 13% of the decrease in EPL), while the patent pendency period dropped by 1.1 years (representing 27% of the decrease in EPL).

1. Data to be used in the calculation of effective patent life

(a) The lists of drugs

In order to evaluate the effective patent life of pharmaceutical innovations in relation to the drug development process, one needs to focus primarily upon new molecules (new chemical entities) as they are approved for the first time for human therapy in the U.S. The

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* - OTA used this as the basis of a figure for their report.

FDA's lists of NDA approvals are the starting point for this study. However most of the drugs on those lists are not NCEs and so do not qualify for our analysis. For recent years, FDA's "Class 1" drugs are close to satisfying our inclusion criteria, but each drug still needs careful screening. Additional criteria are required to keep the study focused on therapeutic new-drug development. For example, we excluded diagnostic agents, vaccines, surgical sutures, contact lenses, devices, new salts, esters or combinations of already-approved molecules, and disinfectants.

In most cases there was no problem in determining which NDA approvals for NCEs to include, because it was obvious which were the new drugs. However there were a few drugs with special histories or uses on which judgment was required. For example, our criteria excluded purified streptokinase for intravascular injection and sodium nitroprusside, since neither is an entirely new drug.

(b) Drug development and patent data

The drug-development data we used were straightforward, consisting of the first NDA approval date for the NCE.

The patent data; importance of the compound patent:

In studying patents in relation to the process of drug discovery and development, we were primarily interested in the original discovery of the NCE. We therefore searched for the original compound patent for each NCE. Of the main types of patent, the compound patent is the one most closely related to the discovery of the compound. It is also usually the one that provides the main protection and confers market exclusivity (See OTA Report; p.52.) The composition patent, used for example for a particular mixture or formulation, can also confer market exclusivity.

The other two types of patent are the method-of-use and process-of-manufacture patents. As pointed out in the OTA report and in the recent statement by the Commissioner of Patents and Trademarks,* these last two types are not nearly as strong as the compound patent in conferring market exclusivity. Because the initial use and process for making the compound are generally disclosed in the compound patent, this information falls in the public domain on the expiration of the compound patent and can be used by anyone. In addition to the original process disclosure accompanying the compound patent, the ease of discovering alternate processes--together with the existence of foreign or concealed manufacturing processes in violation of existing process patents--serve to defeat market exclusivity as the result of process patents alone. In the case of use patents, it is possible for a new and different use to be patented for an existing compound, and such a use patent could outlast the original product patent with its disclosed use. However, such a use patent could only provide market exclusivity if the active ingredient had no other substantial use.

In short, process and use patents normally do not provide any more useful information on EPL for the original discovery than does the compound patent. One should therefore generally use the compound patent where it exists.

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* - In his statement of November 12, 1981, before the Subcommittee on Courts, Civil Liberties and the Administration of Justice of the House Judiciary Committee (p. 7), Commissioner Mossinghoff discussed the several types of patents in some detail. He observed that full market protection of a particular product depends primarily on the product patent itself and upon its effective term rather than upon successive use or process patents.

Drug and Patent Data

The list of drugs and patents for the years 1976 through 1981 are shown in Appendix D. The patent data refer to the compound patent where one exists; 85% of the drugs had compound patents. Where there was no compound patent, the earliest alternate patent was used. The type of patent, date of issue, and patent number are shown against the drug name in these lists.

(c) Method of calculating mean Effective Patent Life (EPL)

The Effective Patent Life of each drug is the time from NDA approval to expiration of the patent. Because there are several different types of patents, there is more than one value for mean EPL. The following procedure was used to calculate a range of mean EPL values that reflect these different patents.

In the first set of calculations, if the drug was not patented or if the patent had expired prior to NDA approval, EPL was taken as zero. If the patent was still pending as of January 1982 (as it was for two drugs), it was arbitrarily assumed to be a compound patent that will issue on December 31, 1982.

Results of mean EPL calculations for each year are shown in the Table underneath the list of drugs for that year. The means were calculated by the class of the patent listed, cumulated in the following order of patent type as shown under the heading "Patents Considered": compound, composition, use, and process patent. The calculations were performed first with denominator equal to the class size ("Mean EPL of Class") and repeated with denominator equal to the total number of drugs approved that year ("Mean EPL Whole Year"). In the former case, drugs lacking the relevant type of patent are excluded, while in the latter case they are counted as having zero EPL of this type. EPL is expressed in years.

If the original patent had expired before NDA approval, the next patent (where available) was substituted (see "Remarks" column) and the calculations repeated. These new mean values are shown in parentheses next to the corresponding unsubstituted mean values.

Finally, the above calculations were repeated after excluding drugs that had no patents or for which the patent was expired or pending. This value, labeled "Unexpired Patents Only," is the figure used in the paper by M. Eisman and W. Wardell (1981), because it usually gave the most cautious value for EPL.

Graphs of average EPL values by year are shown on the last pages of Appendix D and summarized in Table I (see page 22).

Current length of EPL

The Subcommittee has asked me to prepare the best estimate of Effective Patent Life over the past five years to date. Our data for each drug, and results of the EPL calculations for each of the years 1976-1981 are shown in Appendix D and summarized below.

Interpretation of Results

As shown in the tables in Appendix D, the above calculations give a range of EPL values that depend on which patents are considered. Taking compound patents only and averaging over all drugs approved each year, the mean EPL for the years 1976-1981 ranged from 6.8 years to 8.5 years. Adding in the composition, use and process patents shown in the lists, and substituting the next available patent for those that had expired prior to NDA approval, increased the EPL range up to 7.1 to 10.8 years;

however, full protection is not necessarily conferred for the additional period. EPL based on "Unexpired Patents Only" ranged from 7.3 to 11.4 years.

There was a downward trend in EPL over the six-year period, and the values for 1981 are the lowest that have been observed. In 1981 the average Effective Patent Life for compound patents had declined to 6.8 years.

(Question 2) Pharmaceutical Innovation: How is innovation best measured?

I have given considerable thought and research effort to this subject and have published two papers on it (B2 and B3).

"Innovation," in this context is the process of transforming new technical knowledge and invention into medical reality. To measure innovation comprehensively one would need to measure both the quantity and the quality of innovation. Measures of quantity are fairly easy to make: the number of new molecules entering human testing, or reaching the market, are obvious and simple measures of quantity. Measuring the quality or therapeutic value of an innovation is very difficult, and there is no reliable method of doing so. (B2, B3)

There are a number of reasons for this difficulty. First, there is no common scale of measurement. For example, we do not have good methods for comparing the value of a new biochemical treatment for a rare form of adrenal cancer with a new sleeping pill that may have less hangover than an existing one; or for comparing a new antidepressant having fewer cardiac side effects with a new treatment for testicular cancer that produces less nausea than existing ones; or for comparing a new drug that stops sexual aggression in men with one that stops vasospastic angina pectoris. Each of these new drugs--and I have used real examples--is very important to different groups of patients; but we have no scale for measuring whether one innovation is more "important" than another. In the cases I have described, it is obvious that all these innovations can be "important," even in a life-or-death sense. Some are vitally important to just a few people; others are important to many people. In medicine, I do not think we really need a scale of therapeutic importance; however the absence of a reliable measuring stick does make it difficult, in a sense even impossible, to measure the quality of innovative output of an entire nation's pharmaceutical industry.

The second reason that makes it difficult to measure the quality of innovation is that it is impossible to foresee all of a new molecule's pharmacologic or therapeutic properties--either beneficial or toxic--at the time of synthesis, or at the time of entry into clinical testing. Even after the completion of clinical trials when the drug is marketed, major aspects of therapeutic value often remain undetermined.

Many of the most important advances in pharmaceutical innovation and medical therapy occur only through observation of patients taking drugs after they have been marketed for a completely different indication.[*]

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[*] - Examples of such discoveries include some of the most important therapeutic advances of the past three decades: all the main classes of psythotherapeutic drugs (the major tranquilizers and both types of antidepressants), the thiazide diuretics for diabetes insipidus; the antiparkinsonian action of amantadine; the anti-inflammatory action of steroids and of phenylbutazone; the anti-gout action of allopurinol; the antiarrhythmic action of phenytoin and lidocaine; the uricosuric action of probenecid; acetazolamide for glaucoma and epilepsy; diazepam for status epilepticus; and the probable protective effects of platelet modulators (including aspirin) against myocardial infarction and coronary death; the use of aspirin in preventing stroke; and the nonsurgical closure of patent ductus arteriosus in premature babies by indomethacin.

Professor John Oates has described this as the Type II pathway of drug discovery, to indicate that the empirical discovery of new uses for existing drugs is as important as the discovery of new molecules themselves.

A classic example of this phenomenon, the empirical discovery of new uses, is the discovery that the beta-blocker family of drugs can lower blood pressure, treat thyroid symptoms, prevent migraine and prevent heart attacks and sudden coronary death. All of these actions were unsuspected when the drugs were originally approved for the market. Just how important this pathway of discovery can be was illustrated by the recent NIH report that the beta-blocker drug propranolol could prevent at least 6,500 deaths a year from heart attacks in the U.S. alone. In some cases, such discoveries are made years after the drug's approval for the original use (e.g. 13 to 16 years in the case of propranolol's effect in preventing heart attacks and coronary death).

This key pathway of discovery--the observation of therapeutic effects after the drug has been introduced to the market--is particularly important in therapeutic areas where the science and the animal models are least capable of making reliable predictions of a drug's effects in man. The important point to be made here, however, is simply that such unpredictable developments in innovation make even the best estimates of therapeutic value uncertain until years after marketing.

Therefore, based on my own research and experience, I conclude that the best measure of innovative research activity presently available is the number of NCEs introduced into human testing; and that the best measure of research output is the number of NCEs reaching the market.(B2,B3)

There are, to be sure, several other useful indirect measures that bear on the measurement of innovation. As described in my response to Question 3 below, dealing with fluctuation in innovation, these include the increase of research and development costs and time required for a new drug's discovery and introduction, the concentration of R&D activity among larger multinational firms, and the amount of U.S. firms' R&D activity carried out at home versus abroad.

(Question 3) To what extent has pharmaceutical innovation fluctuated during the period 1962-present?

Over the years since 1962, despite a large increase in biological knowledge, U.S. pharmaceutical innovation has shown adverse trends (either absolute or in relation to other countries) in at least six respects:

1. The number of U.S.-originated NCEs entering clinical research and receiving marketing approval has declined by 75%.
2. The proportion of foreign-originated NCEs licensed and acquired by U.S. firms has nearly doubled.
3. The length of time that elapses between synthesis of a new molecule and marketing approval has nearly doubled.
4. The costs of R&D per new drug introduction have increased substantially.
5. There has been a movement of R&D activity abroad by U.S. firms.
6. There has been a decline in effective patent life for new pharmaceuticals.

I shall comment on some of the above items on which we have done research at this point, and will deal with patent life in detail in the other responses.

A. Declining Numbers of NCEs

NCEs are the basic units of pharmaceutical innovation. Numbers of NCEs can serve as an indicator of innovative activity at two stages in the drug-development process: the stage of research or clinical testing and the stage of entry to the market.

At the stage of entry to the market

Compared with the pre-1960 level, the yearly number of new chemical entities (NCEs) introduced onto the U.S. market has declined sharply over the past two decades. During the 1950s, an average of 36 NCEs received NDA approval each year. In the early 1960s this rate declined by 60% to 20 per year, and subsequently to 10 per year. Overall, from 1963 to 1980 we averaged 14 NCEs per year in this country. In 1981 the number increased to over 20.

At the stage of research (investigational drugs)

Several studies done by the Center address the issue of fluctuation in pharmaceutical innovation and development at the investigational-NCE level.

The number and source of NCEs first tested in man were analyzed to study the flow of NCEs into initial clinical testing by U.S. firms. This study covered the period 1958 through 1979.(B6, Figure 1) (Data on investigational drugs prior to 1963 when the IND requirement was instituted have not been available until now.)

This study was based on survey responses from the nine major U.S. pharmaceutical firms which could provide data extending back to 1958. These firms are responsible for approximately 50% of all U.S. NCE pharmaceutical activity. We focused on self-originated NCEs (i.e. those originated by the company engaged in the testing.)

The average annual number of NCEs first administered to man in the 5-year period 1975-1979 has declined by about 75% from the comparable figure in the period 1958-1962. This decline occurred in two stages. First, there was a drop of over 60% in the number of self-originated compounds entering clinical research around the year 1962. This was followed by a second drop, of nearly 50% in the mid-1970s.

As would be expected, the 1962 decline in investigational NCEs was followed by a reduction in the number of new drugs of U.S. origin reaching the market. This reduction persisted until 1970. It is obviously important to know whether the success rates (i.e. the proportion of self-originated NCEs taken into man or filed as INDs which ultimately reach NDA approval) have risen or not over this period. As far as I know this has not been examined before. It is a difficult question to answer even when one has the data. We are currently analyzing our data to examine this point, and are getting various results. By the simplest analyses, success rates have remained relatively constant, at around 10%, since the early 1960s. (Even this figure is rather favorable overall, because anti-infectives have a higher average success rate--approximately 17%. If anti-infectives are excluded, the remainder of U.S. self-originated NCEs have a success rate of less than 7% after the point of IND filing.) But by a more sophisticated mathematical analysis that looks at survival distributions, we have recently (just last month) got some indications that the success rate is actually rising. It will take some more work to tell whether this is true or just due to an artifact such as a changing pattern of pharmacologic classes.

If the success rates do not change, we can predict that, beginning in the early 1980s, there will probably be a further reduction in U.S.

innovations reaching the market as a result of the mid-1970s decline in NCEs entering clinical research. This decline will occur unless some radical, unprecedented increase is forthcoming in the success rates of compounds presently in research; conversely it would be obscured if a backlog of accumulated compounds were to be approved over this period.

B. U.S. Licensing of Foreign-Originated NCEs

From the patient's point of view it does not matter where a drug has been discovered, provided that important drugs become available for use in the U.S. In this sense, the licensing or direct marketing of useful discoveries from abroad is to be encouraged. But licensing patterns do provide a sensitive method of evaluating the relative importance of U.S. firms' own discoveries (and their hopes about discovery) to their total research efforts.

While U.S. innovation has declined, U.S. firms have turned increasingly to the licensing of foreign drug discoveries. As I stated earlier, this has been particularly true of smaller U.S. firms, whose research is now nearly 50% dependent on licensed and acquired compounds. (In the mid-1970s this figure was approximately 25%.) Overall, 80% of compounds licensed and acquired in this country are foreign discoveries.

In summary, the number of new drugs marketed by the U.S. pharmaceutical industry has declined markedly since the early 1960s. Of even greater concern is the current decline in the number of U.S. self-originated investigational NCEs. This recent decline could foreshadow a further erosion of the U.S. output of new pharmaceuticals for the market in the future.

C. Time required for drug development

In addition to the above-described decline in NDA approvals and IND filings over the past 18 years, the total time required for the development of a successful new drug (from synthesis of the molecule to U.S. NDA approval) has nearly doubled. During the five-year period 1963-68 the drug development period averaged 7.2 years. During the period 1975-80 the comparable figure was 12.8 years.* As shown in Table 1, this 5.6 year increase in the total development time is due mainly to longer preclinical and clinical testing phases, i.e. those regulated by the IND requirements. The time required for the NDA review has not changed so much.

Conclusion about the current state of innovation

Based on the above measures it is obvious that pharmaceutical innovation in the U.S. is declining. Furthermore, the decline is occurring despite unprecedented scientific advances which would be expected to have increased it and despite expanding research and development budgets and efforts.

This paradox is not generally appreciated, so it is worth emphasizing here. On the one hand a "golden age" of biomedical science continues: for nearly 30 years advances in techniques and knowledge have been flowing at a rate that is unprecedented in human history. To cite just a few examples, advances in methods such as gas and liquid chromatography, mass spectometry, radioimmunoassay, and immunologic purification techniques have enabled us to separate and identify compounds with a sensitivity and specificity that is breathtaking, even to those of us in the field. This has led to dramatic advances in our understanding of

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* - In using 5-year averages, the slope of the underlying trend is underestimated.

TABLE 1

DEVELOPMENT TIMES (MEAN YEARS) OF NCE-NDA APPROVALS IN THE U.S.*

Time Period	Total Time[1]	Preclinical Phase[2]	Clinical Phase[3]	NDA Review[4]
1963-68	7.2	2.1	2.7	2.0
1969-74	9.7	2.5	4.6	1.6
1975-80	12.8 (15.2)	3.2 (5.1)	5.9 (7.5)	2.1 (2.4)

---

[1] - Time in years from synthesis of molecule to NDA approval.

[2] - Time in years from synthesis to date taken into man.

[3] - Time in years from the date first taken into man until NDA submission.

[4] - Time in years from NDA submission to NDA approval.

---

* - This Table is a working version based on all NCE NDA approvals, both self-originated and licensed/acquired, except for missing data and outliers which cause a discrepancy between the total time and the sum of its parts. Missing data occur mainly in the date of synthesis for licensed or acquired compounds, since the U.S. licensee often did not know the early history of a compound originated abroad. The data for clinical time and NDA review time are the most complete. The outliers consist of a number of drugs in the overall population that took an extraordinarily long time (even decades) at some phase of drug development and are hence markedly atypical. These outlier values have been excluded from the main results shown. If they are included, the values for the period 1975-80 become those shown in parentheses in the Table. It is clear that in the case of non-normal data like the ones in this population, the median might be a preferable measure of central tendency; we are currently examining this.

the body's function in health and disease, and in the mechanisms of disease processes and drug actions. Today we take for granted things we had not heard of just a few years ago: e.g. the enkephalins and numerous synaptic transmitters in the brain; the role of prostaglandins and leukotrienes in inflammation and asthma; and the role of intracellular messengers in all cells. Increasingly, diseases are coming to be defined in terms of disordered intracellular biochemistry, and numerous therapeutic approaches, including pharmacologic approaches suggest themselves. The discovery phase of biological research has never been more productive. As Dr. Donald Fredrickson, then NIH Director, said early last year:

> Never has there been a comparable period of growth in the knowledge of living things. The current revolution in life sciences is not a simple, linear projection of the growth curve in knowledge for the past century. A striking (shift) in that growth has occurred, amounting to a geometric progression of available information... We are on the threshold of some unusual transformation in health practices, agriculture, and industry. (C26)

But after the discovery phase, there is the final narrow funnel--the drug development process--through which all promising new pharmacologic therapeutic candidates must pass before sick people can tangibly benefit from them. This development process consists of three parts, all of which are subject to regulation: the preclinical (chemistry and animal) portion, the clinical (IND) portion, and the NDA review portion. Of course it is right and necessary that the process should be regulated for safety, but it is undeniable that the regulatory process has caused a bottleneck of time, cost, and effort. This dilemma was well recognized over five years ago in the Report of the President's Biomedical Research Panel (April 1976):

> Human beings have within reach the capacity to control or prevent human disease. Although this may seem an

> overly optimistic forecast, it is, in fact, a realistic, practical appraisal of the long-term future.
>
> There do not appear to be any impenetrable, incomprehensible diseases. This, in itself, represents the major advance for biomedical science, and it is a change which has occurred only within the past 25 years. (C10)

The report also acknowledged the major advances of biomedical science, in words similar to Dr. Frederickson's, but then identified the transfer of information and technology, and in this context the regulatory process, as a special problem. The Panel's report stated:

> Meanwhile, there is a different kind of hazard to public health, posed by the prolonged delays and great costs of developing new and potentially useful drugs which the FDA's own protective systems have imposed. In some respects, the agency has become a formidable roadblock. While it is clearly beyond our charge to propose ways for improvement of the FDA, the problem is there, and we are obliged to cite it in the context of this report. (C10)

Under the heading "Pharmacological Sciences Overview," the report identified the areas of "greatest promise" and the "impasse areas." The areas of greatest promise include some of the major medical problems that we currently face, among them cardiovascular disease, proliferative diseases, drug design, control of drug dosage and its delivery to specific targets, pharmacology of genetic engineering, quantification of risk-benefit assessments of important old and new drugs, and therapy for neuromuscular disease.

Conversely, under the heading of "impasse areas," the barriers raised by the regulatory process are singled out for particular attention:

> There is a clear impasse arising between society's desire for new and better drugs and the barriers society is erecting to their development and introduction. These barriers, based on a valid desire to improve the standards of safety and efficacy and to assure ethical control in clinical evaluations,

> increase developmental costs. There is a real danger of bringing the development process and access to clinical resources to a halt.
>
> Many feel that the American public is being denied new drugs currently available abroad because of excessive FDA requirements. (C10)

Thus, the panel's conclusions emphasize what most scientists know and is still true today: that biological knowledge has never advanced at a quicker rate than it has in recent times, that the prospects have never been more promising for therapeutic advances, but that the development process, including regulatory controls is a roadblock to the therapeutic exploitation of this basic knowledge.

I would say the situation is essentially the same as the panel saw it in 1976, although I would not attribute it all to the FDA; it is rather the entire system that has become too cumbersome. This is now generally understood in most circles.

(Question 4) To what extent would pharmaceutical innovation be affected by patent life extension?

It may not be possible to obtain hard data on this point and therefore the answer becomes a matter of judgment. The following judgment is based on my general knowledge, the suppositions underlying the Constitutional mandate for the patent system and some basic points from our own studies that are relevant.

We became interested in this issue because, as discussed previously, we noticed the increasing time required for drug development, particularly at the clinical phase. We assumed that this would have an effect on patent life and we confirmed that the effective patent life was indeed declining. We also found that the causes of this decline included a lengthening of the preclinical time and a quicker issuing of the patent (i.e. shorter pendency) in addition to the expected dominant effect of the lengthening clinical development time.

One cannot fail to be concerned over the long and increasing time now required for the overall drug development process which now approaches 13 years or even longer. We are concerned too about the corresponding erosion of patent life, and the substantial proportion of NCEs whose compound patents have nearly expired by the time they reach the market.

It is obvious that patents provide a major protection for a company's investment in research, and that the erosion which has occurred has diminished this protection. The protection--at least, if based on the compound patent which has been the subject of our studies--is much less than envisaged under the patent act, and substantially less than it was even 15 years ago.

If we agree that the patent system promotes innovation and encourages investment in risky technological ventures, then, it seems to me, we can also presume that the erosion of the effective patent life of pharmaceutical patents is an erosion of the patent incentive. Put conversely, restoration of patent life would be a stimulus to pharmaceutical investment and innovation. While the size of the stimulus ultimately will depend upon industry's perceptions and decisions, I believe that the expectation of a more normal patent life will have a salutory impact on these decisions. The exact amount of restoration time required to spur innovation cannot be fixed theoretically. Moreover it is not necessarily important in my view to determine precisely why patent life is being eroded. Even if all the erosion were due to non-regulatory factors, the problem of disincentive must be dealt with if our society is to benefit in practical therapeutic terms from the dazzling advances that have been made in the biomedical sciences.

SUMMARY AND CONCLUSIONS

Studies performed at our Center and elsewhere provide firm evidence that innovation in the U.S. pharmaceutical industry has declined. Indications of this include the drop in the number of new chemical entities being studied; the licensing of a greater proportion of NCEs from abroad, particularly by smaller firms; and the marketing of fewer NCEs of U.S. origin. If present trends continue, it is unlikely that pharmaceutical innovation will ever return to the higher levels of the past.

With reference to patents, analyses based on very cautious assumptions show that there has been a marked decline in effective life of the compound patent for drugs. This is entirely to be expected from the increase that has occurred in the time from synthesis to marketing approval. Since research and development (and the concomitant investment decisions necessary to implement them) are based on expectations of future gain, changing patent duration will certainly be one consideration in such decision-making, and will in turn affect the prospects for innovation. (See C13, C14 and C25)

The purpose of this statement has been to answer the questions about patents and pharmaceutical innovation posed by the Subcommittee, and to describe relevant findings and methodology from our own studies and those of others. I believe that our studies on drug development, and the decline in effective patent life, provide relevant information for the Subcommittee's consideration. The studies themselves do not, of course, address the social and policy issues of whether the patent law's protection should be restored, or by how much. My own opinion on the latter subject is offered in response to the Subcommittee's question. In short, while our patent study did not recommend any specific course of action, I hope it provides information needed for discussion of these issues.

APPENDIX A

Biographical Statement

William M. Wardell, M.D., Ph.D.

William M. Wardell is Associate Professor of Pharmacology and Toxicology, Assistant Professor of Medicine, and Director of the Center for the Study of Drug Development, at the University of Rochester School of Medicine and Dentistry, Rochester, New York.

He began his medical education in New Zealand and completed it on an Oxford Commonwealth Medical Scholarship in England, graduating M.D. from the University of Oxford where he also obtained an Honors Degree in Physiology and a Ph.D. in Pharmacology. After medical and surgical internships in England and New Zealand, he became a Clinical Pharmacologist on the Faculty of the University of Otago Medical School, Dunedin, New Zealand, and the Toxicology and Clinical Pharmacology Research Unit of the New Zealand government's Medical Research Council. He came to the University of Rochester Medical Center in 1970 on a Merck International Fellowship in Clinical Pharmacology before taking up his present position.

His research interests include clinical pharmacokinetics and pharmacodynamics; the design and methodology of clinical trials; clinical research on drugs for pain, and drugs for preventing myocardial infarction and cardiac death; adverse drug reactions and interactions; studies of drug utilization; and the role of government, industry and other parties in the development and regulation of drugs and in the practice of medicine at national and international levels.

He is a Vice President of The American Society for Clinical Pharmacology and Therapeutics and Vice-Chairman (formerly Chairman) of its Committee on Government Affairs. He is also a member of the National Council on Drugs.

The Center for the Study of Drug Development

Department of Pharmacology & Toxicology
University of Rochester
School of Medicine and Dentistry
601 Elmwood Avenue
Rochester, New York 14642

1850

Dr. Lasagna stated the general purpose of the Center as follows:

"The Center for the Study of Drug Development will devote its energies to the exploration of the problems that keep drug development from being optimally beneficial to the public. A basic objective is to study the entire process of how drugs are discovered, evaluated, developed and used. Important considerations are the points where science and public policy come together, including regulation and economics. On the whole, basic research has been of special interest to the academic community, while development has been the job of industry. Our Center hopes to bring these two sectors, and government, together. Government is particularly crucial because of the way drugs are regulated, and the effects of that regulation on the processes of discovery and development. We hope to provide significant public service and to display the kind of scholarship to be expected from a center based at a first-rate university."

Louis Lasagna, M.D., Chairman of the Department of Pharmacology and Toxicology, and Professor of Medicine, at the formal dedication of the Center for the Study of Drug Development, on May 18, 1976.

Dr. Margaret Mead, past President of the American Association for the Advancement of Science, Chairman of its Board, and Curator Emeritus of the American Museum of Natural History, chatting with W. Allen Wallis, Chancellor of the University of Rochester

Dr. Mead concluded her dedicatory address with these characteristic remarks:

"So I think the inauguration of this Center is a very exciting event. I think you've got just about the hottest potato you could have—which is the way to do this! When I'm working on international relations between two countries who are trying to be allies in a war and are not doing very well, I don't study the areas where they agree. I study the areas where they don't agree, pick out the things they say about each other that are disastrous, and then try to find out how we can make that work. So the fact that you picked such a hot potato—which I hope the University of Rochester Medical School and the Chancellor and everybody is delighted about—will mean that you have a better chance of solving some of these problems than if you picked out something more pedestrian, even though something more pedestrian might have more immediate pay dirt that things like this do not have."

The operating budget of the Center is derived in part from government grants and contracts, in part from donations from the private sector, and in part from private foundations. The Center conducts and supports research bearing on drug development and will sponsor the publication of research findings as well as monographs reviewing the status of important problems in the field. The work is done on a project basis.

There is a small in-house staff of research and secretarial assistants, data management and statistical consultants, and a link with the University's Graduate School of Management. Their work is supplemented, on a project basis, by studies done by contract or grant with experts both within and outside the University.

The Center will consider support for projects involving drug development and regulation, economics and public policy. INDIVIDUALS INTERESTED IN SUCH SUPPORT SHOULD SUBMIT BRIEF PROPOSALS PLUS A BUDGET AND TIMETABLE FOR THE WORK.

William M. Wardell, M.D., Ph.D., Associate Professor of Pharmacology and Toxicology and Director of the Center for the Study of Drug Development

Examples of the Center's Publications*

Wardell, W., Hassar, M. and Lasagna, L. *The Rate of New Drug Discovery. The Output, Flow, and Regulatory Disposition of New Chemical Entities Produced by the U.S. Pharmaceutical Industry Since 1962.*

Lasagna, L. *Consensus Among Experts: The Unholy Grail.*

Hutt, P. *Balanced Government Regulation of Consumer Products.*

Karch, F. and Lasagna, L. *Evaluating Adverse Drug Reactions.*

Lasagna, L. *Dawn's Early Light: A Flickering Flame.*

Roll, G.F. *Of Politics and Drug Regulation.*

Schmidt, A. *Some Homework is Needed.*

Herzog, J. *Recurrent Criticisms: A History of Investigations of FDA.*

Morgan, J. *Watching the Monitors: "Paid" Prescriptions, Fiscal Intermediaries and Drug-Utilization Review.*

Lasagna, L. *Drug Discovery and Introduction: Regulation and Over-Regulation.*

Lasagna, L. *Current Status of International Drug Regulation.*

Kessler, I. *Putting Reason Into Regulation.*

Hansen, R. *Comments on the Proposed Change in the FDA's Trade Secrets Policy.*

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*CENTER PUBLICATIONS consist of original papers, working papers and reprints. Publications in the academic literature are not included here.

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For further information:

William M. Wardell, M.D., Ph.D., Director
Center for the Study of Drug Development
University of Rochester Medical Center
601 Elmwood Avenue
Rochester, New York 14642
(716) 275-2466

APPENDIX B

Published Papers

1. Eisman, M.M. and Wardell, W.M.: The decline in effective patent life of new drugs. Research Management XXIV(1):18-21, 1981.

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Excerpts from Work in Progress

6. Graph from: May, M.S. and Wardell, W.M.: New drug development during and after a period of regulatory change: Research activity of major United States pharmaceutical firms, 1958-1979. Study performed under NSF grant # DAR79-17602.

7. Graphs from: Wardell, W.M., May, M.S. and Trimble, A.G.: New drug development by United States pharmaceutical firms with analysis of trends in the acquisition and origin of drug candidates (1963-1979). Study in progress under NSF grant # DAR79-17602.

Table 5A: Source of Approved NCEs Marketed by U.S. Owned Firms Stratified by Firm-Size (1)

	1963-1968	1969-1974	1975-1980
% Self-Originated			
Small	50.00	51.72	41.67
Middle-sized	55.56	26.67	52.63
Large	77.27	80.00	83.33
% Acquired from U.S. Sources			
Small	20.59	17.24	22.22
Middle-sized	0.00	26.67	21.05
Large	4.55	0.00	0.00
% Acquired from Foreign Sources			
Small	29.41	31.03	36.11
Middle-sized	44.44	46.67	26.32
Large	18.18	20.00	16.67

Table 5B: Source of INDs Filed by U.S. Owned Firms Stratified by Firm-Size (1)

	1965-1969	1970-1974	1975-1979
% Self-Originated			
Small	74.19	69.72	56.00
Middle-sized	74.24	85.71	78.57
Large	96.39	93.67	89.74
% Acquired from U.S. Sources			
Small	7.26	3.67	4.00
Middle-sized	4.54	4.40	1.79
Large	2.41	0.00	0.00
% Acquired from Foreign Sources			
Small	18.55	26.61	40.00
Middle-sized	21.21	9.89	19.64
Large	1.20	6.33	10.26

(1) Patterns of innovative ability of U.S.-owned pharmaceutical firms located in the United States were studied as a function of firm size by ranking the firms according to their total domestic U.S. pharmaceutical sales for 1977-1978 as described and listed in the 1978 edition of the Medical Market Place Guide. Based on this ranking, the firms were stratified into three groups, designated as large (four firms), middle-sized (six firms) and small (eighteen firms in the case of the NDA analysis and seventeen firms in the case of the IND analysis), corresponding to the top, middle and bottom thirds of total sales; respectively. (SOURCE: Center for the Study of Drug Development, Rochester, New York.)

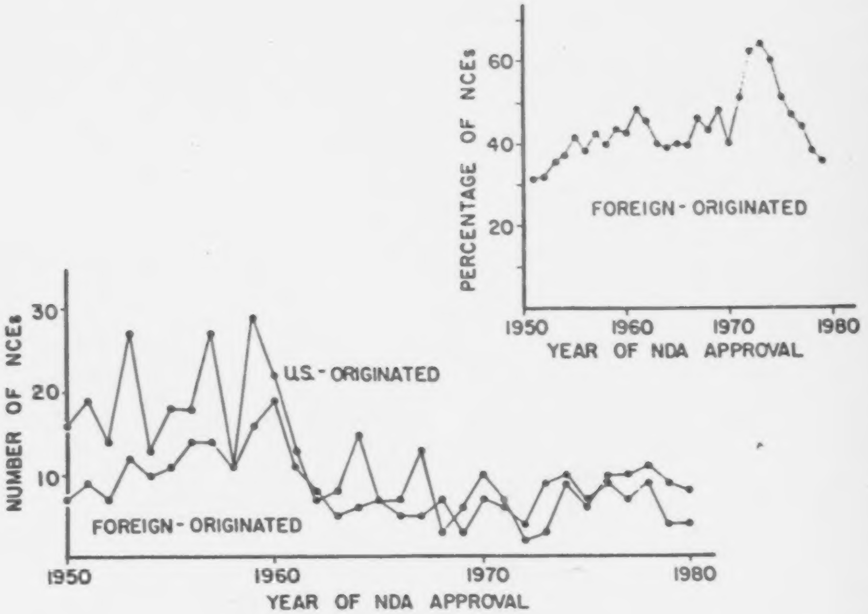

Figure 4. Number of U.S. approved NDAs marketed by U.S.-located firms between 1950 and 1980 by year of NDA approval. The data were stratified by the source or national origin of the NCEs based on questionnaire responses made by approximately 92% of the pharmaceutical firms located in the United States. National origin refers to the nationality of the firm that originally synthesized, owned and/or developed the NCE. U.S.-originated NCEs were therefore NCEs that were either self-originated by U.S.-owned firms or licensed/acquired from U.S.-owned firms by other U.S.-owned firms or by foreign firms. Similarly, foreign-originated NCEs were NCEs that were either self-originated by foreign-owned firms, or licensed/acquired from foreign-firms by U.S.-owned firms or by other foreign firms. In the upper insert, the percentage contribution of foreign-originated NDA approvals is described as a 3-year moving average by year of NDA approval. (SOURCE: Center for the Study of Drug Development, Rochester, New York.)

APPENDIX C

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APPENDIX D: DATA ON NDA APPROVALS, PATENTS, AND EFFECTIVE PATENT LIFE - 1976-1981

Data: Drugs consist of all therapeutic new chemical entity (NCE) NDA approvals by year.

Patent data and calculations refer primarily to the compound patent where one exists; 85% of the drugs had compound patents. Where there was no compound patent, the earliest alternate patent was used. The type of patent, date of issue, and patent number are shown against the drug name in the following lists. These data are the best available to us as of January 29, 1982.

Method of Calculating Mean Effective Patent Life (EPL)

The Effective Patent Life of each drug is the time from NDA approval to expiration of the patent. Because there are several different types of patents, there is more than one value for mean EPL. The following procedure was used to calculate a range of mean EPL values that reflect these different patents.

In the first set of calculations, if the drug was not patented or if the patent had expired prior to NDA approval, EPL was taken as zero. If the patent was still pending as of January 1982 (as it was for two drugs), it was arbitrarily assumed to be a compound patent that will issue on December 31, 1982.

Results of mean EPL calculations for each year are shown in the Table underneath the list of drugs for that year. The means were calculated by the class of the patent listed, cumulated in the following order of patent type as shown under the heading "Patents Considered": compound, composition, use, and process patent. The calculations were performed first with denominator equal to the class size ("EPL of Class") and repeated with denominator equal to the total number of drugs approved that year ("EPL Whole Year"). In the former case, drugs lacking the relevant type of patent are excluded, while in the latter case they are counted as having zero EPL of this type. EPL is expressed in years.

If the original patent had expired before NDA approval, the next patent, where available, was substituted (see "Remarks" column) and the calculations were repeated. These new mean values are shown in parentheses next to the corresponding unsubstituted mean values.

Finally, the above calculations were repeated after excluding drugs that still had no patent listed or for which the patent was expired or pending. This value, labeled "Unexpired Patents Only," is the one used in the paper by M. Eisman and W. Wardell (1981), because it usually gave the most cautious value for EPL.

Graphs of average EPL values by year are shown on the last pages.

Summary and Interpretation of Results

As shown in the following tables, the above calculations give a range of EPL values that depend on which patents are considered. Taking compound patents only and averaging over all drugs approved each year, the mean EPL for the years 1976-1981 ranged from 6.8 to 8.5 years. Adding in the composition, use and process patents shown in the lists, and substituting the next available patent for those that had expired prior to NDA approval, increased the EPL range up to 7.1 to 10.8 years; however, full protection is not necessarily conferred for the additional period. EPL based on Unexpired Patents Only ranged from 7.3 to 11.4 years.

There was a downward trend in EPL over the six-year period, and the values for 1981 are the lowest that have been observed. In 1981 the average Effective Patent Life for compound patents had declined to 6.8 years.

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S T A T I S T I C A L   A N A L Y S I S   S Y S T E M     10:18 MONDAY, FEBRUARY 1, 1982

                    NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                              YEAR OF NDA APPROVAL: 1976

   INGREDIENT                       NDA DATE   PAT DATE    PAT NUM    PAT TYPE  EPL(YRS)     REMARKS

 AMIKACIN SULFATE                   07/12/76   12/25/73   3,781,268  COMPOUND    14.5
 BECLOMETHASONE DIPROPIONATE        05/12/76   04/04/67   3,312,590  COMPOUND     7.9
 DANAZOL                            06/21/76   06/02/64   3,135,743  COMPOUND     4.9
 ETIDOCAINE HCL                     08/30/76   05/21/75   3,862,321  COMPOUND    15.7
 FENOPROFEN CALCIUM                 03/15/76   08/17/71   3,600,437  COMPOUND    12.4
 LACTULOSE                          03/25/76   08/12/69   3,461,204  USE         10.4
 LOMUSTINE (CCNU)                   08/04/76       .      NONE                    0.0  NO PATENTS
 LOPERAMIDE HCL                     12/28/76   01/30/73   3,714,159  COMPOUND    13.1
 MICROFIBRILLAR COLLAGEN HEMOSTAT   08/26/76   07/03/73   3,742,955  COMPOUND    13.9
 NAPROXEN                           03/11/76   09/09/75   3,904,682  COMPOUND    16.5
 PRAZEPAM                           12/14/76   06/29/65   3,192,200  COMPOUND     5.5
 PRAZOSIN HCL                       06/23/76   05/12/70   3,511,836  COMPOUND    10.9
 SOMATROPIN                         07/30/76       .      NONE                    0.0  NO PATENTS
 TICARCILLIN DISODIUM               11/09/76   11/01/66   3,282,926  COMPOUND     7.0
 TOLMETIN                           03/24/76   08/14/73   3,752,826  COMPOUND    14.4
 VIDARABINE                         11/26/76   10/26/71   3,616,208  PROCESS     11.9


      PATENTS CONSIDERED                     MEAN EPL (YRS)     MEAN EPL (YRS)
                                               OF CLASS           WHOLE YEAR

   COMPOUND PATENTS ONLY                         11.4               8.5

   COMPOUND OR COMPOSITION                       11.4               8.5

   COMPOUND, COMPOSITION, OR USE                 11.3               9.2

   COMPOUND, COMPOSITION, USE, OR PROCESS        11.4               9.9

   UNEXPIRED PATENTS ONLY                        11.4
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                                  STATISTICAL  ANALYSIS  SYSTEM      10:18 MONDAY, FEBRUARY 1, 1982

                                  NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                                           YEAR OF NDA APPROVAL: 1977

                                NDA DATE   PAT DATE     PAT NUM    PAT TYPE   EPL (YRS)     REMARKS
  INGREDIENT

AZATADINE MALEATE               03/29/77   06/20/67    3,326,924   COMPOUND        7.2
BACLOFEN                        10/07/77   10/27/69    3,471,548   COMPOUND        9.0
CARMUSTINE (BCNU)               03/07/77   06/07/77    4,028,410   PROCESS        17.3
CIMETIDINE                      08/16/77   04/13/76    3,950,333   COMPOUND       15.7
CLEMASTINE FUMARATE             02/25/77   07/09/63    3,097,212   COMPOUND        3.4
CLOCORTOLONE PIVALATE           08/22/77   04/24/73    3,729,495   COMPOUND       12.7
COLESTIPOL                      04/04/77   09/19/72    3,692,895   USE            12.5
CYCLOBENZAPRINE HCL             08/26/77   07/08/69    3,454,643   COMPOUND        8.9
DESOXIMETASONE                  02/28/77   07/30/63    3,099,654   COMPOUND        3.4
DIFLORASONE DIACETATE           09/14/77   09/14/76    3,980,778   COMPOUND       16.0
DINOPROSTONE                    08/23/77   08/10/71    3,598,858   COMPOUND       11.0
DISOPYRAMIDE                    08/31/77   12/21/65    3,225,054   COMPOUND        5.3
ETIDRONATE DISODIUM             09/01/77   08/08/72    3,683,080   COMPOSITION    11.9
LORAZEPAM                       09/30/77   01/03/67    3,296,249   COMPOUND        6.3
PROBUCOL                        02/01/77   04/27/71    3,576,883   COMPOUND       11.2
QUINESTROL                      10/11/77   12/01/64    3,159,543   COMPOUND        4.1
TAMOXIFEN                       12/30/77   12/31/82    PENDING     COMPOUND       22.0   PATENT DATE ASSUMED


                                              MEAN EPL (YRS)    MEAN EPL (YRS)
      PATENTS CONSIDERED                         OF CLASS          WHOLE YEAR

                                                   9.7               8.0
COMPOUND PATENTS ONLY
                                                   9.9               8.7
COMPOUND OR COMPOSITION
                                                  10.0               9.4
COMPOUND, COMPOSITION, OR USE
                                                  10.5              10.5
COMPOUND, COMPOSITION, USE, OR PROCESS
                                                   9.7
UNEXPIRED PATENTS ONLY
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                        S T A T I S T I C A L   A N A L Y S I S   S Y S T E M     10:18 MONDAY, FEBRUARY 1, 1982

                                  NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                                           YEAR OF NDA APPROVAL: 1978

    INGREDIENT                    NDA DATE   PAT DATE     PAT NUM    PAT TYPE  EPL(YRS)      REMARKS

  ASPARAGINASE                    01/10/78   08/03/71    3,597,323   PROCESS      10.6
  BRETYLIUM TOSYLATE              07/18/78   06/05/62    3,038,004   COMPOUND      0.9
  BROMOCRIPTINE                   06/28/78   08/14/73    3,752,814   COMPOUND     12.1
  BUTORPHANOL TARTRATE            08/22/78   06/25/74    3,819,635   COMPOUND     12.8
  CALCITRIOL                      08/17/78   10/10/72    3,697,559   COMPOUND     11.1
  CEFADROXIL                      02/17/78   01/13/70    3,489,752   COMPOUND      8.9
  CEFAMANDOLE NAFTATE             09/27/78   02/08/72    3,641,021   COMPOUND     10.4
  CEFOXITIN                       10/18/78   10/27/81    4,297,485   COMPOUND     20.0
  CISPLATIN                       12/19/78   12/04/79    4,177,263   USE          18.0
  DESMOPRESSIN ACETATE            02/19/78   02/24/70    3,497,491   COMPOUND      9.0
  DIFENOXIN/ATROPINE              07/14/78   02/29/72    3,646,207   COMPOSITION  10.6
  DIMETHYL SULFOXIDE              04/04/78   12/22/70    3,549,770   USE           9.7
  DOBUTAMINE                      07/18/78   10/19/76    3,987,200   USE          15.3
  METOPROLOL TARTRATE             08/07/78   12/21/76    3,998,790   COMPOUND     15.4
  NATAMYCIN                       10/30/78   07/01/75    3,892,850   COMPOUND     13.7
  SULINDAC                        09/27/78   04/04/72    3,654,349   COMPOUND     10.5
  TIMOLOL MALEATE                 08/17/78   04/11/72    3,655,663   COMPOUND     10.7
  UROKINASE                       01/10/78   .           NONE                      0.0  NO PATENTS APPLICABLE
  VALPROIC ACID                   02/28/78   06/13/67    3,325,361   COMPOSITION   6.3


                                                   MEAN EPL (YRS)       MEAN EPL (YRS)
        PATENTS CONSIDERED                           OF CLASS             WHOLE YEAR


     COMPOUND PATENTS ONLY                              11.3                  7.1

     COMPOUND OR COMPOSITION                            10.9                  8.0

     COMPOUND, COMPOSITION, OR USE                      11.5                 10.3

     COMPOUND, COMPOSITION, USE, OR PROCESS             11.4                 10.8

     UNEXPIRED PATENTS ONLY                             11.4
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                        S T A T I S T I C A L   A N A L Y S I S   S Y S T E M     10:18 MONDAY, FEBRUARY 1, 1982

                                  NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                                           YEAR OF NDA APPROVAL: 1979

   INGREDIENT                     NDA DATE   PAT DATE     PAT NUM    PAT TYPE  EPL (YRS)     REMARKS

AMCINONIDE                        10/18/79   08/07/62    3,048,581   COMPOUND     0.0   USE PATENT (4,158,055--6/12/79)
CARBOPROST TROMETHAMINE           01/09/79   04/17/73    3,728,382   COMPOUND    11.3
CEFACLOR                          04/04/79   12/09/75    3,925,372   COMPOUND    13.7
CYCLACILLIN                       09/18/79   01/05/71    3,553,201   COMPOUND     8.3
DAUNORUBICIN HCL                  12/19/79   12/14/76    3,997,662   COMPOUND    14.0
ISOFLURANE                        12/18/79   10/20/70    3,535,425   COMPOUND     7.8
METOCLOPRAMIDE                    02/07/79   04/06/65    3,177,252   COMPOUND     3.2
METYROSINE                        10/03/79   01/13/59    2,868,818   COMPOUND     0.0   COMPOS. PAT (3,362,879--1/9/68)
MINOXIDIL                         10/18/79   08/12/69    3,461,461   COMPOUND     6.8
NADOLOL                           12/10/79   01/27/76    3,935,267   COMPOUND    13.1
NALBUPHINE                        05/15/79   07/16/68    3,393,197   COMPOUND     6.2
TICRYNAFEN                        05/02/79   09/11/73    3,758,506   COMPOUND    11.4
TRIMIPRAMINE MALEATE              06/12/79   05/29/51    2,554,736   COMPOUND     0.0   PAT. EXPIRED--NO OTHER PATS.


       PATENTS CONSIDERED                         MEAN EPL (YRS)      MEAN EPL (YRS)
                                                     OF CLASS           WHOLE YEAR

   COMPOUND PATENTS ONLY                           7.4  ( 8.7)        7.4  ( 7.4)

   COMPOUND OR COMPOSITION                         7.4  ( 8.4)        7.4  ( 7.8)

   COMPOUND, COMPOSITION, OR USE                   7.4  ( 9.1)        7.4  ( 9.1)

   COMPOUND, COMPOSITION, USE, OR PROCESS          7.4  ( 9.1)        7.4  ( 9.1)

   UNEXPIRED PATENTS ONLY                          9.8
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                              S T A T I S T I C A L   A N A L Y S I S   S Y S T E M     10:18 MONDAY, FEBRUARY 1, 1982

                                     NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                                               YEAR OF NDA APPROVAL: 1980

      INGREDIENT                 NDA DATE    PAT DATE     PAT NUM     PAT TYPE   EPL(YRS)    REMARKS

      AMOXAPINE                  09/22/80    08/01/72    3,681,357    COMPOUND      8.9   HYDRATE FORM
      CALCIFEDIOL                08/05/80    09/03/74    3,833,622    COMPOUND     11.1
      CINOXACIN                  06/13/80    06/13/72    3,669,965    COMPOUND      9.0
      MAPROTILINE HCL            12/01/80    08/27/68    3,399,201    COMPOUND      4.7
      MECLOCYCLINE               05/30/80    05/16/61    2,984,686    COMPOUND      0.0   PAT. EXPIRED--NO OTHER PATS FOUND
      MECLOFENAMATE NA           06/25/80    04/11/67    3,313,848    COMPOUND      3.8
      OXAMNIQUINE                07/23/80    06/28/74    3,821,228    COMPOUND     10.9
      RITODRINE                  08/29/80    11/12/68    3,410,944    COMPOUND      5.2
      SISOMYCIN SO4              10/29/80    09/23/75    3,907,771    COMPOUND     11.9
      TRIFLURIDINE               04/10/80    08/17/65    3,201,387    COMPOUND      2.4
      ZOMEPIRAC NA               10/28/80    08/14/73    3,752,826    COMPOUND      9.8


        PATENTS CONSIDERED                          MEAN EPL (YRS)     MEAN EPL (YRS)
                                                       OF CLASS          WHOLE YEAR

      COMPOUND PATENTS ONLY                              7.1               7.1

      COMPOUND OR COMPOSITION                            7.1               7.1

      COMPOUND, COMPOSITION, OR USE                      7.1               7.1

      COMPOUND, COMPOSITION, USE, OR PROCESS             7.1               7.1

      UNEXPIRED PATENTS ONLY                             7.8
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S T A T I S T I C A L   A N A L Y S I S   S Y S T E M    10:18 MONDAY, FEBRUARY 1, 1982

                 NCE DRUGS AND PATENTS, BY YEAR OF NDA APPROVAL

                         YEAR OF NDA APPROVAL: 1981

    INGREDIENT                 NDA DATE   PAT DATE     PAT NUM    PAT TYPE  EPL(YRS)    REMARKS

  ALBUTEROL                    05/01/81   02/22/72   3,644,353   COMPOUND     7.8
  ALPRAZOLAM                   10/16/81   10/19/76   3,987,052   COMPOUND    12.0
  ALPROSTADIL                  10/16/81   12/18/62   3,069,322   COMPOUND     0.0  PAT. EXPIRED--NO OTHER PATS.
  AMILORIDE HCL                10/05/81   04/13/67   3,313,813   COMPOUND     2.5
  ATENOLOL                     08/19/81   05/16/72   3,663,607   COMPOUND     7.7
  BETHANIDINE SULFATE          05/29/81   02/02/65   3,168,562   COMPOUND     0.7
  BUPRENORPHINE                12/29/81   03/18/69   3,433,791   COMPOUND     4.2
  CAPTOPRIL                    04/06/81   08/08/78   4,105,776   COMPOUND    14.3
  CEFOTAXIME NA                03/11/81   05/01/79   4,152,432   COMPOUND    15.1
  ESTRAMUSTINE                 12/24/81   01/07/67   3,299,104   COMPOUND     2.0
  FLUNISOLIDE                  09/24/81   03/24/64   3,126,375   COMPOUND     0.0  PROCESS PAT (4,273,710--6/16/81)
  GEMFIBROZIL                  12/21/81   07/04/72   3,674,836   COMPOUND     7.5
  HALAZEPAM                    09/24/81   02/25/69   3,429,874   COMPOUND     4.4
  KETOCONAZOLE                 06/12/81   12/31/82   PENDING     COMPOUND    18.6  PATENT DATE ASSUMED
  MEZLOCILLIN                  09/21/81   08/10/76   3,974,142   COMPOUND    11.9
  MOXALACTAM DISODIUM          10/06/81   02/06/79   4,138,486   COMPOUND    14.3
  NIFEDIPINE                   12/31/81   12/23/69   3,485,846   COMPOUND     5.0
  PIPERACILLIN                 12/29/81   09/05/78   4,112,090   COMPOUND    13.7
  SUCRALFATE                   10/30/81   03/11/69   3,432,489   COMPOUND     4.4
  SULFADOXINE                  10/28/81   05/03/66   3,249,603   COMPOUND     1.5
  TEMAZEPAM                    02/27/81   01/03/67   3,296,249   COMPOUND     2.8
  TRAZODONE                    12/21/81   04/30/68   3,381,009   COMPOUND     3.4
  VERAPAMIL                    08/12/81   07/19/66   3,261,859   COMPOUND     1.9


                                           MEAN EPL (YRS)   MEAN EPL (YRS)
       PATENTS CONSIDERED                     OF CLASS        WHOLE YEAR

    COMPOUND PATENTS ONLY                   6.8  ( 7.1)     6.8  ( 6.8)

    COMPOUND OR COMPOSITION                 6.8  ( 7.1)     6.8  ( 6.8)

    COMPOUND, COMPOSITION, OR USE           6.8  ( 7.1)     6.8  ( 6.8)

    COMPOUND, COMPOSITION, USE, OR PROCESS  6.8  ( 7.5)     6.8  ( 7.5)

    UNEXPIRED PATENTS ONLY                  7.3
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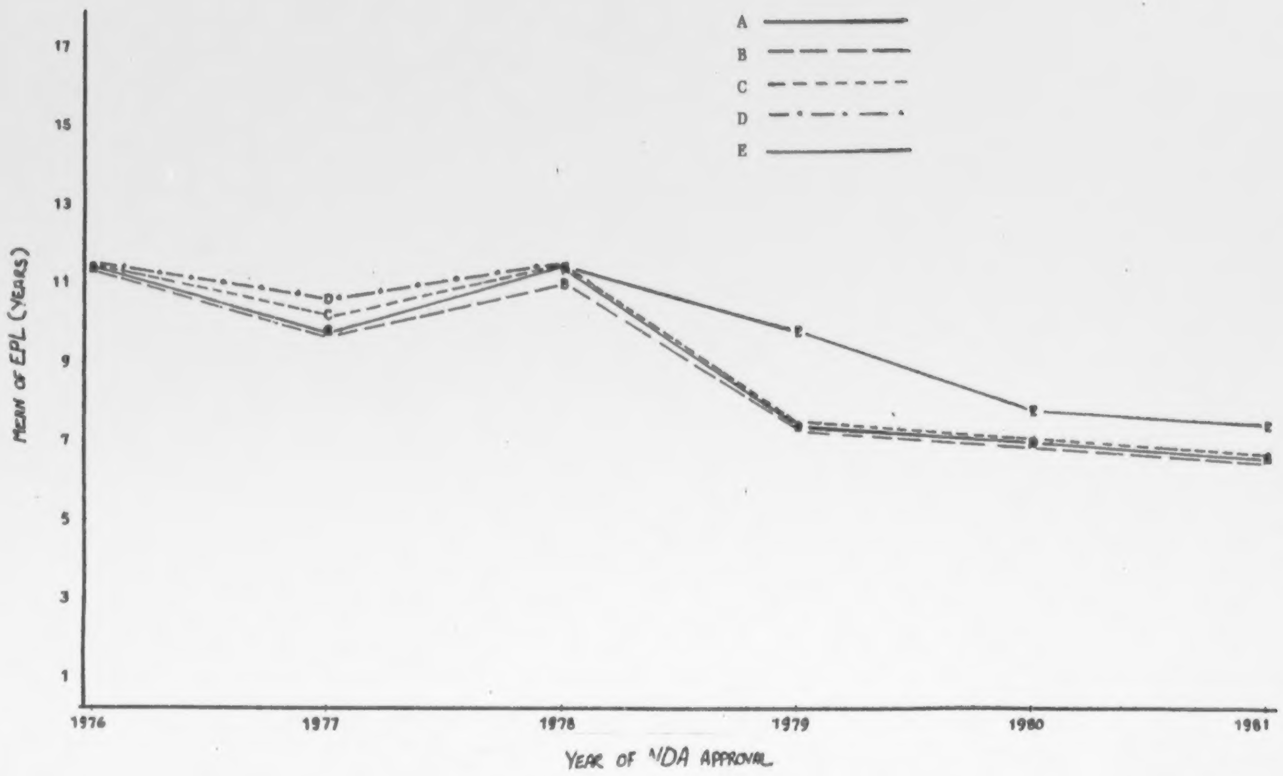
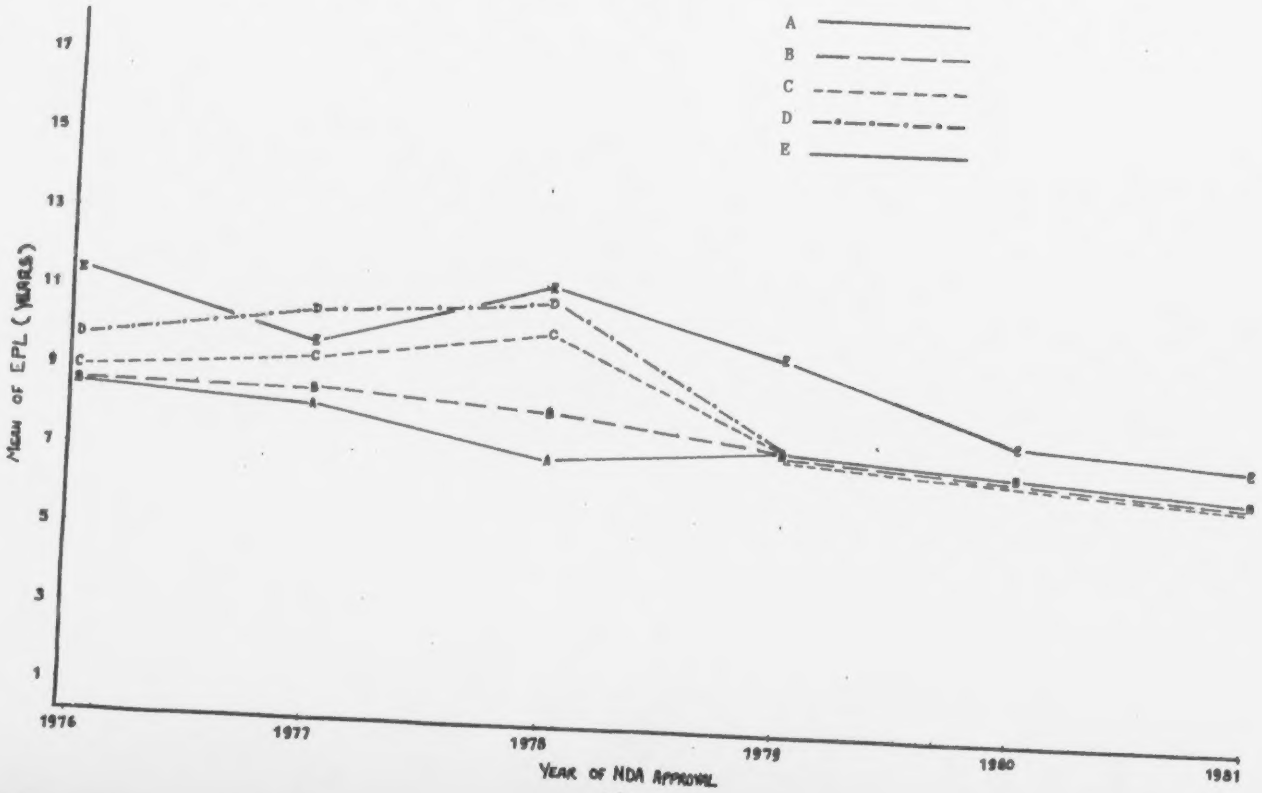
PLOT OF MEAN EPL FOR COMPOUND (A), COMPOUND AND COMPOSITION (B), COMPOUND, COMPOSITION AND USE (C), COMPOUND, COMPOSITION, USE AND PROCESS (D), AND UNEXPIRED PATENTS (E).



PLOT OF WHOLE YEAR EPL FOR COMPOUND (A), COMPOUND AND COMPOSITION (B), COMPOUND, COMPOSITION AND USE (C), COMPOUND, COMPOSITION, USE AND PROCESS (D), AND UNEXPIRED PATENTS (E).



Mr. **Gore**. Yes.

Dr. **Wardell**. That is probably the most important part of my presentation.

Mr. **Gore**. Thank you very much, and I appreciate your testimony.

Do you believe there is an increasing trend toward licensing of pharmaceuticals in this country?

Dr. **Wardell**. Oh, certainly. This is in my answer to question 3. Page 20 of my statement, and appendix B4, B7-2, and B7-7. Could we defer that a little, and I will pick up any questions of that type.

Mr. **Gore**. Defer it until when? What do you have in mind?

Dr. **Wardell**. Let me then turn to——

Mr. **Gore**. You have completed your statement, have you not?

Dr. **Wardell**. Yes. I could finish there now, certainly.

Mr. **Gore**. OK. Have you completed your statement?

Dr. **Wardell**. Mr. Chairman, it depends how short on time you are. I could certainly finish there.

Mr. **Gore**. Yes. We would appreciate that for a variety of reasons. The time pressure. But basically your answer is yes, there is an increasing trend toward licensing of pharmaceuticals?

Dr. **Wardell**. Yes.

Mr. **Gore**. What do you think the implications of this trend are for pharmaceutical innovation?

Dr. **Wardell**. First, if you look at the component of licensed and acquired products in the research portfolios of U.S.-owned firms, they have now reached approximately one-third of all new chemical entity IND filings. That has happened over about the last 5 years. Conversely, the proportion self-originated has gone down from a value of about 80 percent throughout the 1960's to two-thirds now. If you look at success rates; that is, whether these IND's are going to make it to an NDA, success rate for the self-originated ones is 10 percent, and success rate for the acquired ones—because they may have been marketed abroad before being filed as IND's—we find is 28 to 30 percent. So acquired NCE's have a three times higher success rate. Couple that with the fact that the self-originated new molecules have declined very greatly; even in the 1970's they dropped by 50 percent, while the acquired ones overall are remaining constant. Thus, we find that not only is the proportion of acquired NCE's being studied by U.S.-owned firms rising, but the chances of their success is also three times as great as for self-originated NCE's. I think it is fairly obvious that we will see a much higher proportion of foreign-originated compounds reaching the market through U.S. firms in the future.

Now then, you can ask where these licensed and acquired compounds are coming from? We have got some studies of that. In fact, they are shown in the figures of my appendix B-7. I will just summarize them here. The United States as a source of licensed and acquired products for other U.S. firms is declining, Europe is declining a bit, and Japan is the one that is rising. Next you can ask, into what sort of U.S. firms are they going? The fascinating thing we found is that while the large firms have increased their dependence upon licensed and acquired compounds from about 5 or 10 percent to 15 percent over the last 5 or 10 years, and while medium-sized firms have bobbled around a bit and do not show a trend, the small firms are now as much as 50-percent dependent on licensed and acquired products.

Mr. **Gore**. Now, in your original study, did you leave any drugs out of that study due to pending periods at the Patent Office?

Dr. **Wardell**. That were still pending when approved?

Mr. **Gore**. Yes.

Dr. **Wardell**. Yes.

Mr. **Gore**. When what you regarded as excessive pendency at the Patent Office?

Dr. **Wardell**. That is described in the methodology for computing the mean labeled "unexpired patents only." In the case of this mean, but not the others, anything that was zero or pending was excluded. Because there were more zeros—patent expired—than pending, for most years including something that did not have a patent, would have brought the mean down even further.

Mr. **Gore**. So there were some excluded?

Dr. **Wardell**. Yes.

Mr. **Gore**. Were there some similar to the ones excluded toward the end that were included in the early part of the analysis?

Dr. **Wardell**. The compound is not——

Mr. **Gore**. With excessive pendency periods?

Dr. **Wardell**. The only ones that were excluded by the definition of whether a patent existed or not were some that were pending.

Mr. **Gore**. But the definition served to exclude some at the end and include some at the beginning—do you know what I am referring to?

Dr. **Wardell**. No. Could you give me an example?

Mr. **Gore**. Oral contraceptives is one example.

Dr. **Wardell**. I do not believe——

Mr. **Gore**. Were they included in the beginning part of the analysis? I believe they were.

Dr. **Wardell**. I would have to check on that. There are almost no oral contraceptives approved since the early sixties that are new molecules.

Mr. **Gore**. The point is that in the early part of your analysis they were included during the early period with the long pendency period, but drugs with a similar regulatory profile were excluded, at least one with a very long pendency period, excluded at the end.

We will hold the record open and let you comment on that.

Dr. **Wardell**. Mr. Chairman, you have to list what the drugs are. We had rules for handling these, and they do not depend on how long the pendency is, if the patent has been issued. If you could list the drugs——

Mr. **Gore**. We will do that for you, and we will hold the record open for inclusion of that material and your considered response to it.

[The information follows:]

One needs to distinguish between the terms "pendency" and "pending," and between calculations of the EPL versus its components.

In calculating overall EPL, no drugs were excluded on the basis of the patent pendency period. Drugs that had patents expired prior to the NDA approval, or still pending as of January 1982 (two drugs), were excluded for one type of calculation only, namely the value labeled "Unexpired Patents Only." This is fully described on page 1 of Appendix D, in the paragraph headed "Method of Calculating Mean Effective Patent Life."

In calculating a component of patent life such as the pendency period, it is occasionally necessary to exclude outlier values to avoid biasing the mean. This was done in the case of two drugs as described in Footnote C, page 21, of our original paper. As shown there it applies to the calculation of pendency period, not to the calculation of Effective Patent Life.

Mr. GORE. Now, do you believe that any portions of the FDA regulatory review process are unreasonable?

Dr. WARDELL. I believe the law is a very good law and the requirements in the law for safety and efficacy are very reasonable. I believe the regulations of May 8, 1970, that define the requirements for the well-controlled clinical trials that are needed to yield substantial evidence are also very reasonable. I think problems have arisen in the implementation of the law and the regulations, and I think the day-to-day practices have often gone beyond the wording of the law and the regulations and the intent of the Congress. So where I have seen examples of that that are unreasonable, I think some practices at times are unreasonable, but not the legislative or the regulatory framework, at least as far as the regulations of May 8, 1970, go.

Mr. GORE. All right. Let me yield to my colleague, Mr. Walker.

Mr. WALKER. Thank you, Mr. Chairman.

If I understand the substance of what you have concluded from your studies and from statistics that you have looked at, you have determined that in fact the innovation in the industry has been harmed by some series of decisionmaking that goes on; is that correct?

Dr. WARDELL. The facts are that the level of innovation has dropped. The causes—I have been involved in research on the causes for some time. If you want to apportion causation to the different factors, I find it very hard to quantitate the role of Government versus industry, versus economics, versus the standards of science. The main fact is that yes, it is much more difficult to create innovation these days.

Mr. WALKER. Based upon your experience prior to this kind of interference, the United States was a world leader would you say in the area of innovation and production of drugs?

Dr. WARDELL. The United States is still very high, but it has dropped on some measures. For example, last month I was looking at a report from the German pharmaceutical industry which showed the United States dropping from first place to fourth place in the last 5 or ten years in terms of monetary value of pharmaceutical exports. That is quite a dramatic figure. I have it here.

Mr. WALKER. Well, could you give us—could you sum up for us what you think is the cause behind that drop in leadership? I realize most of what you have said here is a summation, but could you give us basically a synopsis that says what based upon your research you believe that the problem is that is causing us to lose leadership at least in some categories?

Dr. WARDELL. The whole system, and by that I include the Government and industry, is extremely cumbersome, and I have seen it myself as a clinical investigator. Nine or 10 years ago there were just fewer forms to sign, fewer surveillance procedures, and research was more pleasant. Today, I think even at the clinical investigator level, the amount of paperwork and general policing—the lack of scope for original thinking imposed by the procedures that now need to be adopted—is quite daunting. I know people who will not do drug studies because they do not like it. The system is terribly cumbersome, and I think that and the unreasonable interpretations of the law and regulations in some cases are the causes.

Mr. WALKER. So we can say that as the approval period has gone up, innovation has gone down, based upon your study?

Dr. WARDELL. Yes.

Mr. WALKER. And that anything that would be done that would impact upon that approval period by reducing the approval period would likely produce greater innovation; is that a logical conclusion?

Dr. WARDELL. It would help.

Mr. WALKER. Based upon your expertise, do you have a personal position on H.R. 1937?

Dr. WARDELL. My personal opinion, and this is stated in answer to question 4 that the subcommittee posed for me, is that extending the patent life would increase innovation, although I do not know by how much.

Mr. WALKER. So it is another one of those things that it is hard to come up with quantitative measurements, but you believe that it would have a positive impact of some degree?

Dr. WARDELL. Yes.

Mr. WALKER. Is it not true that the innovator can control when the IND is filed, but cannot control the NDA approval period?

Dr. WARDELL. That is generally true, yes.

Mr. WALKER. So once again, insofar as we modify based upon that reality, we might be able to achieve some positive effects on innovation in the marketplace?

Dr. WARDELL. By what procedure, sir?

Mr. WALKER. Well, by either shortening the NDA approval or by extending the patent period.

Dr. WARDELL. Yes; when you phrase it like that.

Mr. WALKER. Thank you, Mr. Chairman.

Mr. GORE. You just said that innovation has been going down. Are you sure about that? Let us take the years since 1962. We had testimony from the Commissioner, Dr. Hayes, that there is no perceptible pattern of decline in innovation since 1962. We have the report of the Office of Technology Assessment that there has been no decline in innovation. On what do you base your testimony that there has been a decline in innovation?

Dr. WARDELL. Perhaps we could turn to question 3 here, where I have a list of measures. This is on page 17. And these are the ones I had in mind as showing a declining level of innovation, or at least that conditions are becoming more difficult for innovation. The number of U.S.-originated NCE's entering clinical research and receiving marketing approval have both declined by about three-quarters since the early sixties.

Mr. GORE. Well, now wait a minute. You have taken two things and lumped them together there.

Dr. WARDELL. Yes.

Mr. GORE. If you separated them out and you took the ones that have received approval, there has been no decline, has there?

Dr. WARDELL. There was an enormous decline around 1962.

Mr. GORE. You mean from prior to 1962?

Dr. WARDELL. Yes.

Mr. GORE. Of course. That is when the new law went into effect and you had efficacy and you had a lot of drugs before 1962 that did not do anything good, and then they were not approved after 1962. But in the modern era, since 1962, there has been no decline in innovation, has there?

Dr. WARDELL. If you look at marketed drugs, and this is described in the paper that I have labeled appendix B-3, "The Measurement of Pharmaceutical Innovation"——

Mr. GORE. Yes.

Dr. WARDELL. Here is where I looked—excuse me—B-2, "The Measurement of Therapeutic Value." We are looking at the number of new chemical entities labeled "Important and moderate gains." I believe that if you lump those two together, at least according to the rating of the physicians we polled for this——

Mr. GORE. Who is "we"?

Dr. WARDELL. The study we did of——

Mr. GORE. The center?

Dr. WARDELL. Yes; about 3 years ago, I believe there was a decline from about 1960—in fact if you look at figure——

Mr. GORE. From 1960?

Dr. WARDELL. Well, things peaked around 1960, 1961.

Mr. GORE. Things peaked right before the new law. Since 1962, do you have any evidence that there has been a decline in innovation since 1962?

Dr. WARDELL. Well, let us work down my list, Mr. Chairman, because I have given this some thought. If you look for a start at figure 1 and figure 2 on page 85 of the paper in B-2——

Mr. GORE. Yes; I am looking. If you look—there does not seem to be any decline to me in either figure. I mean this is a central issue. The allegation has been made that innovation has declined. Since 1962 there has been no decline. I await any evidence to the contrary.

Dr. WARDELL. First, I believe—I cannot find the exact place, but I believe we did look at the trend in this, and if you look for example at the solid line in figure 1, I believe we have looked at this and there are some indications that based on marketed drugs it is declining, but I will need some time to——

Mr. GORE. We will give you some time. That is not drugs approved at all. That is the number of self-originated NCE's entering clinical testing.

Dr. WARDELL. Figures 1 and 2 of appendix B2 deal with marketed drugs only.

Mr. GORE. Are you looking at the solid line at figure one on 85, page 85?

Dr. WARDELL. Yes.

Mr. GORE. Gee, you may be looking at that different from the way I am. Does that show a pattern of decline from 1962 on? Certainly, if you add the figures from 1976 to 1981, it doesn't.

I don't think it even does here.

Dr. WARDELL. There is a decline in——

Mr. GORE. It is at the same level at the end of the chart as at the beginning of the chart.

Dr. **Wardell**. We do have strong data based on self-originated compounds only that——

Mr. **Gore**. Approved?

Dr. **Wardell**. Yes.

Mr. **Gore**. Where is that? Where is that?

Dr. **Wardell**. I can certainly supply it.

[Information follows:]

This information is now supplied as Appendix B7-8. The number of U.S. self-originated NCE"s brought to the stage of NDA approval declined greatly in 1960-62. For the next 10 years thereafter, i.e. until 1972, there was a further decline, although this was of smaller magnitude and there were relatively large anual fluctuations in the small number of NCE's being approved by that time.

Mr. **Gore**. Dig it up. Let's look at it.

I can't believe that it is not readily available. It is the key to this whole argument.

Dr. **Wardell**. Moving on then, we should now look at self-originated new chemical entities at the point where they are entering clinical research, that is, NCE's which may become new drugs 5 to 10 years down the road. Please look at the appendix B-7, figure 1. This shows new chemical entities entering research, not marketed NCE's. There is a 50-percent decline as recently as the mid-1970's.

Mr. **Gore**. Is that your definition of innovation?

Dr. **Wardell**. The number of new chemical entities is one of the strongest definitions that there are. If you have a better one, I would be very glad to consider it.

Mr. **Gore**. The number of drugs innovated.

Dr. **Wardell**. These are drug candidates that may become drugs. So this is at the point of entry into clinical research, which is a much earlier stage than the point of marketing. You can see here that they are——

Mr. **Gore**. The litmus test is how many are made available to the public. There has been no decline.

Dr. **Wardell**. Well, there has been a decline in self-originated ones. I didn't know you would be asking that question, but I would be glad to supply what we have on that.

Mr. **Gore**. Please supply that for the record.

[See graph now supplied as appendix B-7—8, as described above.]

Mr. **Gore**. Let me ask you another question.

Dr. **Wardell**. Before we leave B-7, let me point out there has been a 50-percent decline in the number of U.S.-originated new chemical entities entering research even since the midseventies.

I think that is quite serious. If that is not accompanied by a rise in success rate—and, as I noted in my statement, it is possible that we might be just beginning to observe a rise in success rate, but no one has noticed this before, it has to be sorted out—it would be very serious.

Mr. **Walker**. Will the gentleman yield?

Mr. **Gore**. Sure.

Mr. **Walker**. There is a chart on page 272 of B-4 which shows a rather dramatic decline in self-originated NCE's, the number of IND's filed, the NDA's submitted, NDA's approved.

As of December 1976, could you talk about that as it relates to the questions that the chairman has been asking because there is a significant decline between 1963 and 1976?

Dr. **Wardell**. Mr. Walker, you are talking about figure 2?

Mr. **Walker**. Figure 2.

Dr. **Wardell**. That is the number of IND filings on new chemical entities.

Mr. **Walker**. IND filing time would be at the time they are actually taking something which they have innovated and moving it toward the marketing process, right? What this shows is that during that period of time those chemicals or those drugs for that period of time have dropped off sharply since 1963?

Dr. **Wardell**. Yes. The differences between figure 1 and figure 2 are that in Figure 1, we are looking at the entire U.S.-owned industry's new molecules first given to man somewhere in the world; and you notice that nearly half of those by 1976 were first given to man abroad.

Figure 2 shows, from the same set of drugs, which ones are coming to the United States as IND's. Figure 2 should decline approximately the same as Figure 1, the difference being those that are tested abroad but not brought into the United States as IND's.

Mr. **Walker**. What this shows additionally it seems to me, is that even though if a case could be made that there has been relative stability in the amount of innovation in this country over that period of time, the fact is that over all the innovation in the world that stable figure results in research innovation in this country relative to the world position because other nations have been innovating at a rate far faster than ours.

In terms of innovation in the world community, we have come steadily downward, is that correct?

Dr. **Wardell**.Yes, Mr. Walker, but this particular study is not a comparative one. We are just looking at the United States. If the rest of the world were also coming down, we might be at the same relative level. But this does show in absolute terms a very profound decline in the number of new molecules produced by the U.S. industry entering human investigation in the midseventies. That was after a decade of stability.

Mr. **Walker**. The fact is there has been a significant increase in the numbers of foreign-innovated drugs that have come into our marketplace?

Dr. **Wardell**. Yes; that is a separate question. I have got data bearing on that.

Mr. **Walker**. That means there is a foreign industry that has done that innovation and introduced it to our marketplace whereas our companies have not done that innovation and introduced it to our marketplace?

Dr. **Wardell**. Correct; the proportion of licensed and acquired drugs reaching our markets is about 50 percent of the total at the present time (see appendix B-7—8).

Mr. **Gore**. It seems to me the incentive to innovate is not some psychological perception of regulation at FDA but profits. What is the company going to get as a result of what it does? Have you noticed a marked decline in the profits of the industry since 1962?

Dr. **Wardell**. We don't have any studies on profits.

Mr. **Gore**. Well, I do. They haven't declined. In fact, the OTA study on page 16 has a table 1 which, without objection, I will put in the record at this point.

[The information follows:]

Table 1.—After-Tax Rates of Return on Average Stockholders' Equity 1956-79 (in percentages)

Year	Pharmaceutical industry	All manufacturing	Year	Pharmaceutical industry	All manufacturing
1956	17.6	12.3	1969	18.4	11.5
1957	18.6	11.0	1970	17.6	9.3
1958	17.7	8.6	1971	17.8	9.7
1959	17.8	10.4	1972	18.6	10.6
1960	16.8	9.2	1973	18.9	12.8
1961	16.7	8.8	1974	18.7	14.9
1962	16.8	9.8	1975	17.7	11.6
1963	16.8	10.5	1976	18.0	13.9
1964	18.2	11.6	1977	18.2	14.2
1965	20.3	13.0	1978	18.8	15.0
1966	20.3	13.4	1979	19.3[a]	16.4
1967	18.7	11.7			
1968	18.3	12.1	1980 (1st 3 quarters)	20.8	13.9

[a] Industrial classifications were changed. The percentage of companies reclassified in the drug industry is unknown.

Note: For the purpose of this table, the pharmaceutical industry is defined as corporations primarily engaged in manufacturing biologicals, inorganic and organic medicinal chemicals, pharmaceutical preparations, and grading, grinding, and milling of botanicals.

SOURCE: Quarterly Financial Reports, U.S. Federal Trade Commission.

Mr. GORE. It shows that the after-tax rates of return on equity have increased and since 1975 it has been a rather steady increase even from 1979 to 1980 when all manufacturing reflected a decline.

In addition, we also just passed a change in the law to give tax credits for current investment in R. & D., providing for a tax credit equal to 25 percent of the increase in R. & D. over the previous 3-year average.

Do you think that might serve to stimulate the amount of money put into R. & D.?

Dr. WARDELL. It sounds as though it would. I don't know what the existing credits are. It is reminiscent of what is happening in Japan, as a matter of fact. So it sounds as though the direction would be up, but I would have to ask an expert on that.

Mr. GORE. That is a far better incentive to innovate, to put money into R. & D. than patent term extension. Patent term extension is not an incentive to increase research and development now, simply a mechanism for assuring companies of greater sales 10 years from now during restored or extended patent life in order to get 0.085 cents of every sales dollar invested in R.& D. at that time.

If you want to create incentives for an immediate increase in investment, in R. & D., then you ought to take the route that the Congress just adopted, the law just taking effect. Indeed, many observers believe that for that reason and for other reasons scientific in nature we are on the verge of a major upturn in the amount of innovation going on in the industry.

You say you don't have any figures on profits. You don't have any reason to dispute the OTA's figures there, do you?

Dr. **Wardell**. Mr. Chairman, I am not an economist. I would refer that question to someone who is.

Mr. **Gore**. OK.

Dr. **Wardell**. Also the question on tax. However, you did mention being on the verge of a breakthrough. I have seen similar statements for at least 5 years——

Mr. **Gore**. Not a breakthrough, an upturn?

Dr. **Wardell**. Everyone has been saying that. The report of the President's Biomedical Commission in 1976, which I quoted in my statement, was saying that. But the upturn hasn't happened.

Mr. **Gore**. I think the upturn in the amount devoted to R.& D. is in fact happening. I cite you an article in Fortune magazine this past fall saying, for example, that Merck is pouring a colossal $280 million into R. & D. this year, nearly four times the amount that it invested in R. & D. 10 years ago.

Eli Lilly's $201 million for 1980 was three times the amount that it invested in 1971. Pfizer's research and expenditure, which quintupled from 1970 to 1980, will grow by nearly 16 percent this year, to around $185 million while Squibb has boosted spending for R. & D. 84 percent in the last 5 years to $91 million.

Sounds to me like there is a lot of incentive. Sounds to me like they are looking at these fantastic profit figures and looking at the flat innovation rate for the last several years since 1962 and decided that it is lucrative for them to greatly increase the amount that they are putting into R. & D.

Dr. **Wardell**. Mr. Chairman, in 1972 Fortune magazine had a very optimistic article on the prostaglandins and how much the Upjohn Co. was investing in them. I haven't seen many prostaglandins coming out. As you heard Dr. Hayes say this morning, there's only two on the market—both, I believe, for premature babies. The market there is not very great.

Mr. **Gore**. The point is, they are spending money to try.

Dr. **Wardell**. And the number of NCE's entering clinical research is going down. It has gone down by 50 percent since the mid-seventies. That was the B-7 figure I showed you and Mr. Walker pointed to.

Mr. **Gore**. I personally don't believe that is the relevant figure. I think there are scientific reasons for that. We will get into that——

Mr. **Walker**. Will the gentleman yield?

I think since the economic argument has been raised it does need to be noted at this point in the record it is irrelevant.

The fact is that the Constitution protects patent rights. It says that there is a need to have patent rights given to an inventor to protect that invention for a certain period of time.

If we take the argument and extend it far enough that somehow this doesn't apply to drug companies as well as to the inventor of the Rubik's cube, I think we have got ourselves a rather indefensible position along the way.

In other words, somebody who comes up with an invention that indeed solves a major disease problem, it seems to me, should have at least as much protection as somebody who invents the latest version of the hula-hoop.

You know, that is the real issue here, rather than the money figure.

I would submit you could send those profits soaring for a short period of time if you would simply eliminate all the R. & D. You can look down through this chart. You could send the profits soaring for a short period of time by simply X-ing that out of your budget.

The problem is, at the end of some fairly short period of time, you would end up with no growth whatsoever in the industry.

Mr. GORE. Reclaiming my time, I think that is a perfectly respectable argument. If one chooses to support the pending legislation for that reason, it is perfectly understandable. The fact is, the Constitution struck a balance between two competing goals. No. 1, to stimulate innovation, and No. 2, to protect the public against unreasonably lengthy exploitation of state enforced monopoly periods.

Now, the Constitution directed the Congress to establish fixed times for patents. The fixed time was established at the current level in 1981 with full recognition that the patent period for a variety of inventions and developments would not be the full 17 years because many inventions patented would not be available from the company for sale to its public at the beginning of the patent period.

There is nothing really new about that. The fact is, the law used to have an extension at the discretion of the Patent Office prior to 1961 that Congress chose to repeal. For the last 121 years, it has been at the 17-year level.

If you want to say that we believe it is important enough to supercharge this industry, this particular industry and give it a lot more money by giving it a longer patent period with all the implications that carries with it—no matter what you believe they are—about price, there are implications, OK., the Congress can do that.

But, if the premise on which the Congress acts is that there has been a decline in innovation and a decline in the attention that companies pay to R. & D. because of this monster called the regulatory process, then the Congress is acting on a false premise because that premise just is not true or there has been no evidence to indicate that it is.

Mr. WALKER. I just want to make certain we get our history correct here with regard to 1861. The compromise struck was between a House version of the bill which said 17 years and a Senate version of the bill which said 17 years with the possibility of a 7-year renewal.

We settled on a—which went even further down the road—it was settled on as 17 years.

Mr. GORE. Fourteen years with a 7-year renewal.

Mr. WALKER. OK. Nevertheless, it was a comedown from that—the 17 year was a matter of compromise. It was to be a flat, firm kind of situation so that I think it needs to be noted for the record that that is what Congress at that time considered to be and previous Congresses have gone along with to be the time that would inspire the innovation.

Mr. GORE. And 120 years have validated our great President Lincoln's judgment in signing that law.

Mr. WALKER. There is no doubt about that. It was probably started in President Buchanan's term, who just happens to be from Lancaster, Pa.

I could do a discourse on President Buchanan, if you like.

Mr. GORE. Let's move on.

Dr. Wardell, thank you very much. We look forward to receiving the additional information. If you can find anything indicating a decline in innovation, we would be most interested in that.

[This is contained in appendix B7, where several such measures of investigational and marketed NCE's are shown.]

Mr. GORE. Our next witness—we will change the agenda in accord with the agreement stated earlier. We would like to call Mr. Peter Hutt, counsel for the Pharmaceutical Manufacturers Association and then we will ask the panel from the Generic Pharmaceutical Industry Association to come up next.

[Witness sworn.]

Mr. GORE. Thank you very much. Welcome to you. We are sorry that your client could not appear here today. I have the greatest respect for Mr. Ingman and we tried to coordinate the date with him several months in advance.

I am sure that it is unavoidable. I am not sure I know the reason. I am sure it is unavoidable.

We are happy to have you here. I would like to note for the record that you have an excellent reputation in the regulatory law industry and PMA is said to have an able advocate. We welcome you.

Let me say that your entire statement is 48 pages in length and we don't want to be discourteous. If there is some way that you might summarize it, it would be helpful. We do not want to be discourteous. We will leave it to your discretion.

In the interests of time, if you could do that, it would be appreciated.

STATEMENT OF PETER BARTON HUTT, COUNSEL, PHARMACEUTICAL MANUFACTURERS ASSOCIATION

Mr. HUTT. Thank you, Mr. Gore. I will indeed shorten the statement. I will also try to indicate where I have omitted material and will try therefore to lead you through the statement.

As you know, Mr. Chairman, and Mr. Walker, I am Peter Hutt. I am appearing today on behalf of the Pharmaceutical Manufacturers Association.

Let me turn on page 1 of my statement immediately to the question of innovation in the pharmaceutical industry.

A recent report of the National Academy of Sciences has defined innovation in the following way: And I will only quote the first sentence: "Economists define technological innovation as the initial commercial application of a new product or process."

In the pharmaceutical industry, innovation in our judgment is best defined or best measured by the number of new chemical entity drugs approved by the Food and Drug Administration for marketing during any particular time. These NCE drugs represent, in the words of the National Academy, "the initial commercial application of a new product or process."

During the period from 1962 to the present, pharmaceutical innovation in the United States has declined substantially.

Figure 1 on page 3 shows the progressive and dramatic reduction in yearly FDA approvals of NCE drugs for use in this country.

As you have pointed out, the big dip occurred between 1950 and 1960, when it held fairly steady to a dramatic reduction beginning in the mid-1960's. The reduction occurred, I believe, starting in about 1960 and was completed in about 1962 or 1963.

Since 1962 or 1963, the number of NCE's approved by FDA, while it has varied from year to year, has shown roughly the same trend and no particular reason can be given for any larger number or smaller number in any particular year.

Why has pharmaceutical innovation dropped off from the fifties and early sixties to the mid-sixties to late seventies? There are two reasons.

Mr. Gore, do you have a question?

Mr. GORE. I will wait until you complete it.

Mr. HUTT. First, drug research is lagging behind the growth rate of the drug industry. Pharmaceutical R. & D. expenditures continue at a fairly steady rate of 12 percent of drug sales. But when these figures are adjusted for inflation—which OTA did not do—it becomes apparent that the rate of pharmaceutical R. & D. in relation to drug sales has been reduced by about one-third in the past 15 years because drug research costs have increased dramatically in relation to drug prices.

This real decline in pharmaceutical R. & D. expenditures is shown in figure 2. That is located on page 4.

I would ask that you quickly take a look at that figure because that is quite dramatic.

This reduction in real R. & D. tracks, to some extent, the figures just given by Dr. Wardell showing that the number of U.S. originated NCE's entering man in the United States has also dropped.

Second, the cost of developing and obtaining approval of an NCE drug has also risen dramatically; regulatory requirements have increased.

It is estimated that about 10,000 candidate drugs are synthesized for every one that actually gets to market. For every 10 drugs that reach the very expensive and time-consuming clinical investigation stage, only one is ultimately marketed. The cost of chemical, animal, and clinical testing of NCE drugs has soared. The time required for FDA approval is more than three times longer than it was 20 years ago. The cost of money, as we all know, has escalated.

As a result, the total amount of investment needed to produce a single approved NCE drug, which has been estimated at about $6 million in 1962, or $16 million in 1980 dollars, and increased to $54 million in 1976, has now reached the almost unbelievable level of $70 million per NCE approved drug.

Thus, from any given level of R. & D. investment by the pharmaceutical industry today, the country realizes fewer NCE drugs than it once did. Coupled with a decrease in real R. & D. investment, it is not surprising that the statistics show a substantial decline in pharmaceutical innovation in the United States today.

I will turn on page 6 to the importance of pharmaceutical innovation.

Mr. Gore, I would suggest I can briefly summarize here. Dr. Hayes and Dr. Wardell, in their testimony, have spoken very eloquently of the need for new lifesaving drugs in this country.

Table 1 on page 6 and table 2 on page 7 show the decline in death rate and disease rate from 1960 to the present, a remarkable improvement for our country. Much of this is attributable to drugs made by PMA member companies. Medicine to achieve the same dramatic results against our current leading causes of death, heart disease, and cancer are now major targets for the pharmaceutical industry.

It is not true that only major new breakthrough drugs contribute to this reduction in morbidity and mortality. We must pursue progress in small, as well as large, increments.

A new drug is not uniformly safe and effective throughout the entire population. Biological variations among people require development of a large armamentarium of drugs to assure that the benefits of pharmaceutical science reach as many as possible.

A number of new drugs although not broadly classified as breakthrough products for society as a whole, are nonetheless of crucial importance to individual patients for the alleviation and cure of their disease. That is why the availability of a wide variety of drugs for any particular disease is so vital to the public health.

Drug prices, drug prices have been one component of health care costs that has remained relatively stable over the last 20 years. While the Consumer price Index has risen 178 percent and health care costs have increased 629 percent, the cost of prescription drugs has increased only 34 percent.

As shown in table III on page 10, the drug share of national health expenditures has declined every year during this past decade and extending even further beyond that.

In an era when the cost of medicare and medicaid threatens the stability of our entire economy, one need only look at the savings from new drug introductions to appreciate how better therapy can produce lower health care costs.

My statement gives examples of that, but I will omit them.

Pharmaceutical innovation thus saves lives, improves the quality of life, and reduces the cost of health care, all at the same time.

It is appropriate to turn to the crucial role of patents in pharmaceutical innovation. Mr. Chairman, you and Mr. Walker have talked about the history of our patent system. I will, therefore, save time and not talk about how important it has been to the American economy.

There is one point beginning in the middle of page 12 that bears some emphasis.

The importance of patent protection obviously increases with the size of the investment needed to achieve innovation in any field. If innovation can be purchased cheaply, patent protection is relatively unimportant.

As the investment cost escalates, however, patent protection becomes far more important.

In the pharmaceutical industry where the cost of an NCE has escalated so dramatically, the assurance of strong patent protection has become increasingly crucial to the future of the industry.

This fact was explicitly recognized in the recent report by the Office of Technology Assessment on patent term restoration.

I will quote only one sentence on page 13 from that: "In view of these facts, research intensive pharmaceutical firms consider patent protection as a prerequisite to innovation."

I cite two other examples of this finding. One is a 1968 GAO report which said that the reason the Government could not exploit its patents, particularly in the pharmaceutical field, was precisely because at that time the Government, for misguided reasons, was not turning those patents over to private enterprise for commercialization.

The industry would not waste time attempting to commercialize a product with no patent protection.

Congress, in 1980, enacted the patent amendments precisely to make sure that Government patents were given to private enterprise to commercialize.

Let me turn then on page 14 to a brief discussion of the drug research investigation and approval process. We have heard a great deal about this process this morning.

The starting point in my judgment is a report that was done by one of your coordinate committees, the House Subcommittee on Science, Research and Technology in 1980.

That report demonstrates the major impact of FDA regulatory requirements throughout the drug development process from the moment a new chemical entity is synthesized until final FDA approval of an NDA. That process is divided into three separate components: Preclinical research, clinical investigation, and NDA approval.

Let me begin with preclinical research.

I will not read all of this, Mr. Chairman, but only highlight various parts.

Before clinical investigation of an NCE may begin, substantial research must be undertaken on the chemical, pharmacologic and toxicologic properties of the chemical in order to meet FDA prerequisites for clinical research.

The report of the House committee stated that those FDA requirements, "* * * affect the type and direction of research and other development activities which must be done once a new chemical entity is identified."

We also point out in footnote 24 that FDA itself has said that preclinical, as well as clinical testing, "* * * is subject to a comprehensive regulatory scheme."

I shall not read, Mr. Chairman, from all of the FDA regulations and requirements. They are laid out for preclinical research on pages 15 and 16. With the length and depth of those requirements——

Mr. Gore. Let me just stop you there.

Very briefly, your citation on the IND seems to refer to the NDA process on 26, footnote 26, talking about——

Mr. Hutt. Yes, but the report points out that the process of development of chemical information about the drug begins at synthesis and travels all the way through to NDA approval. What occurs is disagreement, quite frequently, between the industry and the FDA as to the level of chemistry information that must be included at each stage of that process.

When one files an IND, for example, the IND must contain—and I quote this on page 15:

> A statement of the methods, faciliites, and controls used for the manfacturing, processing, and packing of the new drug to establish and maintain appropriate standards of identity, strength, quality and purity as needed for safety and to give significance to clinical investigations made with the drug.

That requirement means that even at the preclinical stage before one can put the drug into humans, one must have sufficient information about manufacturing procedures, chemical specifications, and chemical analysis to justify to the FDA reviewer that an IND can begin.

Mr. GORE. Sorry to interrupt. Go ahead.

Mr. HUTT. Quite all right, sir.

Accordingly, going back to the top of page 17, it is not surprising that the House committee report found that preclinical research can take 1 to 4 years to complete.

I would emphasize, Mr. Chairman, this is without any delay on the part of the sponsor whatever.

I would state now—and we can pursue this in the questions later—that I know of no basis for OTA's arbitrary time of 2 years for preclinical study.

As I listened to the testimony this morning, it appeared to be a misconception about the nature of preclinical work. Preclinical work that they referred to this morning dealt only with animal studies.

Much of the preclinical work deals with chemical characterization of the drug, initial work of an innovation nature long before you get to animals.

As Dr. Sarett of Merck testified before Mr. Waxman's committee in April, indeed it is sometimes necessary to build a pilot plant to make the drug before you can even begin the animal studies.

Let me turn to clinical investigation. Once adequate preclinical research is completed, an IND can be filed to justify clinical investigation of the new chemical entity in humans.

The amount of information required by FDA to be filed with an IND is extensive. The IND regulations, including the requirements for protection of human subjects, currently comprise some 25 pages in the Code of Federal Regulations. One of the questions that has been raised is the trend in the duration of an IND. I would refer to figure III on page 18 of our statement, Mr. Chairman, which shows the extraordinary increase from 1966 to 1976 in the duration of IND time.

The third stage, turning to page 19, is the NDA approval. After the FDA requirements for preclinical research and clinical investigation are completed, the NDA is submitted to the agency to obtain approval of the drug for marketing. Until that approval is obtained, the drug may not be commercialized.

The statute requires FDA to act upon an NDA within 6 months. The House subcommittee report found that the average NDA approval time was 14 months in 1963, rose to 37.3 months in 1971, dipped to 20 months in 1976, and climbed back up to 35.2 months in 1979.

The vast majority of these NDA's are eventually approved, but the amount of time taken by FDA to review them during which the drugs cannot be marketed, is very significant.

We discuss attempts at improvements.

Mr. Gore, like you, we are very much interested in having FDA improve its drug approval process. We applaud the establishment of the commission you sponsored.

Dr. Crout, Director of the FDA Bureau of Drugs, has pointed out there is only so much that can be done in improving the process.

He states, and I quote him on page 20: "In my judgment, not more than a year or so."

As Dr. Hayes testified this morning, we are stuck with a regulatory drug approval process that will always take a substantial number of years. What does that mean with regard to the gradual erosion of pharmaceutical patent protection?

Congress, of course, has never changed the 17-year patent term for pharmaceutical products. But the Government research, testing, and approval requirements just described have substantially reduced the effective length of that term.

For drug products, therefore, the 17-year patent term has become a legislative figment.

In reality a drug patent has a much shorter effective life. As a result, incentives to invest in pharmaceutical R. & D. have been substantially reduced.

Indeed, they have been cut in half in the last 14 years.

The erosion of effective patent life for pharmaceuticals began about 20 years ago. It coincides with the erosion in pharmaceutical innovation. It is readily apparent that the public has been the loser.

The sick—and particularly the elderly, the people with diseases for which medicine has not yet been developed—have been the real victims of lost patent life and reduced pharmaceutical innovation.

Let me turn, on page 22, to studies on effective patent life.

There is not just one study on this subject, Mr. Chairman. There have been several studies. Indeed, we heard of two more this morning that are not included in our document.

All of these studies show exactly the same trend. Both individually and in combination they confirm a substantial decrease in effective drug patent terms. The effective patent life of the NCE drugs approved by FDA in 1980 was less than half the 17 years provided by Congress.

We review in our statement five studies: the first conducted by Pracon for Hoffman-LaRoche; one conducted by Prof. David Schwartzman; another by Prof. Meir Statman; the study we heard about just from Dr. Wardell, the Eisman-Wardell study; and the PMA study conducted at your request, Mr. Chairman, to provide additional data for the year 1980.

To these I would like to add a sixth and seventh study we heard about today. The sixth study is the OTA study which confirmed without exception the PMA data that were provided to you in November. The seventh study is Dr. Wardell's study which I believe showed a lower patent term for 1981 still, namely, 6.8 years.

In table 4 on pages 24 and 25, we have laid out the data that we provided to you last year.

Mr. GORE. Excuse me. You referred to the OTA study?

Mr. HUTT. The OTA analysis. I am sorry.

Mr. GORE. You said it confirmed the PMA figure?

Mr. HUTT. It did indeed show 7.4 years. They did not find any difference with our data.

Mr. GORE. They took your data?

Mr. HUTT. But they also went back, it is my understanding, and looked at additional aspects. They checked the patents or obtained the data somewhere because they confirmed that the data we had on the patents was indeed the right data.

Mr. GORE. OK. They confirmed it because they got it from you. You gave it to me. I gave it to them. It wasn't an independent corroboration of the data they gave you. It is a minor point.

Please proceed.

Mr. HUTT. There were some differences in specific dates. We inferred they had reasons to have changed those dates.

Mr. GORE. We will get into it in the questioning.

Mr. HUTT. It makes no difference, in any event. No one has suggested that those data are in any way inaccurate.

The most important aspect of this is contained in figure 4 on page 27, Mr. Chairman. We have plotted five of the studies that we mention in our statement from year 1966 to year 1980.

You may add, if you wish, an additional dot on that chart for the year 1981 to add the 6.8 years that Dr. Wardell has found for 1981. That would, of course, be beneath the lowest line on that chart.

What is striking is the congruence of all of these figures. There is not a single one of those five studies that is in any way inconsistent with what I describe, namely a 50-percent reduction in effective patent life, a 50-percent reduction in the incentive produce lifesaving new drugs, since 1966.

Let me turn then to the role of compound, composition, use, and process patents. This has been a matter that I know has been of great interest and concern to a number of people. The recent OTA report addresses this, I think, in a very fair and objective way.

To summarize, under existing law, every patent application, whether for a pharmaceutical product or for some other invention, must disclose the product, a method for using the product, and a process for making the product.

It is important to understand that the initial compound or composition patent application for a new drug, like any other patent application, must disclose a use and a method for making that product. That becomes important later on as we will see.

Once a patent application is filed or granted—whether for a pharmaceutical products, again, or for any other invention—additional patent application may also be filed to cover related new inventions. For example, an entirely new use may be found for a product that had not been described before, or a new process may be found to make the product more cheaply, or with fewer impurities, or in some other safer or more useful way. These subsequent patents, including use patents and process patents, are also important to innovation. Companies must invest substantial resources to develop new uses for, and methods of manufacturing, existing products.

Without the incentives provided by the patent system, these investments surely would be less attractive and perhaps would never be made at all. I give some examples in there, including the most important example I know you are interested in, Mr. Gore, the issue of orphan drug uses that are often discovered after a drug is initially marketed for a primary purpose.

The Patent Term Restoration Act, turning to the bottom of page 29, is designed to restore, at least in part, the effective patent life originally intended by Congress.

This legislation, as we have heard this morning, has been passed by the Senate and is awaiting markup in the House. PMA strongly supports this legislation and urges its enactment as quickly as possible.

I will not go into the details of that bill, Mr. Gore, because you are quite familiar with it.

Turning to the top of page 31, the bill provides a new climate of restored incentive for pharmaceutical innovation. It is justified on grounds not just of innovation, but equally important of fundamental equity as Mr. Shamansky pointed out this morning.

First, it is plainly inequitable for an NCE drug, once approved by FDA, to have an average patent life of 7.4 years, or as we have just heard 6.8 years, when other inventions can obtain an effective patent life of 17 years.

This is not a question of the drug industry asking for special treatment. The bill is designed simply to provide for drugs the same consideration Congress has given to other inventions.

The tax incentives you mentioned a few moments ago, Mr. Gore, were not in lieu of or to replace patent protection. They were in addition to the patent protection that exists for all other products.

Even if the Patent Term Restoration Act is enacted into law, drug patents will continue at a disadvantage. As noted, the legislation allows a maximum of only 7 years patent extension. If it were applied to the NCE drugs approved by FDA during 1980, it would have increased the average effective patent life, I originally thought, to 14.4 years. Based upon the OTA report of this morning, it is only 13.1 years. Certainly it would not have fully restored the 17 years intended by Congress.

It would, in short, be 4 years less, even under the new act, if it were passed tomorrow and were made retroactive which we are not asking.

It would still be 4 years less than the statutory time period granted by Congress to all other inventions.

The legislation thus provides no windfall to the pharmaceutical industry. It merely provides some, but not all, of what has been lost as a result of increased governmental research, testing, and approval requirements during the past 20 years.

On the basis of equity alone, the legislation is fully justified.

Second, and this does reach your point of innovation, we believe the legislation is vitally needed to reinvigorate pharmaceutical investment and thus to help return pharmaceutical innovation to its former stature.

The public interest is best served when new therapies that are safe and effective become available as quickly as possible.

For this to happen, incentives to invest in pharmaceutical research and development must be adequate. The current downward trend in real R. & D. investment in the pharmaceutical industry and in pharmaceutical innovation can only be halted, and hopefully reversed, if the industry perceives—and I emphasize perceives—that a major change in policy has provided new incentives.

I do not agree, Mr. Chairman, that it is simply a question of profit today. It is a question of the industry leaders' perception of future trends. As Dr. Hayes and Dr. Wardell said, what is beginning today will not show up in the pharmacy as an approved NCE drug for perhaps a decade.

One cannot prove—and PMA has never argued that one can prove—with mathematical precision that the Patent Term Restoration Act or the IND/NDA revision effort will in fact result in a specific number of new drugs becoming available that otherwise would be lost to our society. But the chief executives and the research directors of PMA member companies believe that these efforts, if they succeed, will be a major stimulus to new research.

Mr. Chairman, I would like to turn now to the arguments that are made against the legislation primarily those espoused by the Generic Pharmaceutical Industry Association, (GPIA). GPIA cites two principal arguments. First, they contend that the new legislation would result in higher drug prices during the period that the patent is extended.

Second, they contend that the industry is already able to protect its inventions through multiple use and process patents and thus that further legislation is unnecessary. We believe neither of these arguments is valid.

The development of new drugs, and new methods of using and making older drugs, represents the single greatest hope of this country for holding down health care costs.

If one eliminated the new drugs developed in this country during the past 20 years, the cost of health care would have increased far more than it has. Particularly for the elderly and the poor, the development of safe and effective new drugs is essential to assure that all segments of our population receive adequate medical treatment at a reasonable cost.

Moreover, increased incentives for innovation will result in a higher level of pharmaceutical research, development of a larger number of drugs, and thus the marketing of drugs to compete with important existing drugs in order to provide price competition.

This is not mere economic theory. The major new antiulcer drug, Tagamet, for example, was on the market only 4 years before a competitor, Carafate, appeared.

Nor can the industry continually protect a product from competition once the basic compound or composition patent has expired.

As I mentioned earlier in discussing patents, the basic patent must disclose the compound or composition, a method of use, and a method of manufacture. This is the most important thing. Once that patent expires, any competitor is free to market that compound or composition made in the way disclosed in the patent for any use disclosed in that patent.

Many people ask about the subsequent process and use patents? Those new patents could not prevent any competitor from making the product and marketing it in accordance with the specifications and for the uses disclosed in the original expired compound or composition patent.

I would refer you in this connection, because I am not going to read his testimony, to the testimony of the Commissioner of Patents and Trademarks, which is quoted on pages 42 and 43.

He says, again perhaps more eloquently than we have, that the idea of pyramiding or evergreening of patents is simply a fiction.

The attack made upon subsequent user and process patents is an ill-disguised attack upon the basic patent system itself.

I think that was recognized this morning. In substance, these attacks contend that the research intensive pharmaceutical companies either must be content with an effective patent life that is half that granted by Congress to all other industry, or must forego any incentive whatever for developing new uses and new methods of manufacture for existing products.

This approach would be counterproductive and self-defeating. It would single out pharmaceutical products for discriminatory and indeed punitive treatment. It would destroy incentive to develop an improved life-saving drug. It rests solely upon the short-term hope of immediate reduced prices for a few drugs brought in by competition from generic drugs and it would sacrifice the long-term economic health of the pharmaceutical industry and the public health of the country as a whole.

We strongly urge that this shortsighted approach, which would seriously endanger the future of innovation in the pharmaceutical industry, be rejected.

In prior congressional testimony—and we may hear it again today—the GPIA has rested its case primarily upon one table listing 12 important drugs which purports to show that the effective patent protection averages 18.5 years.

For a number of reasons, that table not only offers no persuasive argument against patent restoration, but, indeed—properly analyzed—it supports the PMA position.

First, I must point out the drugs on that table are not the most frequently prescribed drugs in America. They were obviously chosen to show the longest possible patent terms that could be found among all important drugs.

Second, the NDA's for 8 of those 12 drugs were approved prior to 1968. The latest DNA of the 12 was approved in 1978.

In those earlier years—as our chart shows—the effective patent life was, of course, longer than it is today. In short, the GPIA table simply does not address the central issue today; namely, that the effective patent life today on an average is less than 8 years.

Indeed, as we heard a moment ago, it is less than 7 years.

Third, we see the same decreased in effective patent life in the GPIA table as in the studies that we plotted in figure III in our own statement.

The drugs approved prior to 1968 show longer effective patent lives. The drugs approved in 1976 to 1978 show shorter effective patent lives, demonstrating the effect of increased regulatory requirements.

Fourth—and this is perhaps the most important part, Mr. Gore, because we recognize your concern about the effect of the Patent

Term Restoration Act if it were law today—for 7 of those 12 drugs there would be no patent term restoration if the Patent Term Restoration Act had been enacted into law years and years ago. There would be zero time restored. For two drugs, the restoration would be 4 and 6 years, and for three drugs it would be 1 year of patent term restoration.

Why is this? This is because the bill only restores patent protection where it has been lost as a result of the regulatory process.

If no protection is lost, nothing is restored.

If the NDA is approved before the patent is granted, there would be no patent term extension regardless of the extensive regulatory requirements.

In short, the inequity that we are concerned about and that has been created by existing law would be removed under the new legislation.

There could be no possibility of increasing patent protection beyond the 17 years.

Mr. HUTT. I do not wish in my remaining time to read from the OTA report or the views of other Government agencies, but I would like to address myself particularly to the information in the analysis, as we will call it, that was provided this morning by OTA. I think that analysis, for reasons that I will discuss actually supports the PMA position on patent-term restoration.

What we point out in that are four principal facts. Let me state them: First the OTA data show the average regulatory period calculated by them to be from FDA receipt of the IND to FDA approval of the NDA to be 8.3 years for 1980. Dr. Crout has previously testified that that period in his judgment is 7 years. Dr. Hayes repeated that this morning. What we have found by the OTA analysis is that it is a year and a quarter longer than the FDA estimates, and that it is indeed the most significant thing that detracts and takes away from effective patent life.

Second, the OTA data show that if the Patent-Term Restoration Act had been law, the patents for those 12 drugs would be restored an average of 5.7 years.

Mr. Chairman, again I emphasize this is 2½ years less than the average regulatory period calculated by OTA for these drugs. This underscores how conservative the Patent-Term Restoration Act is. It does not compensate for the entire regulatory period.

Third, the OTA presentation confirms, as I said earlier, that the effect of patent life for 1980 is indeed 7.4 years. It may be, as you said, that they accepted our data on that, but in any event they did not disagree with it.

Mr. GORE. That is from the first patent? That is PMA's figure?

Mr. HUTT. Yes.

Mr. GORE. Not for all the patents?

Mr. HUTT. Not on any subsequent compound or use patent.

Mr. GORE. The comparable figure is 8.2?

Mr. HUTT. As I have stated, those subsequent patents would not prevent a generic manufacturer from coming in and making the original drug for the original use and the original process, once that initial patent is expired at the end of 7.4 years.

Mr. GORE. We will pursue it, but it might in fact have that effect.

Mr. HUTT. We can get into that later. Dr. Wardell has provided data which confirm the OTA analysis. Dr. Wardell has shown that 60 percent of the decline in the effective patent life has come in the IND-NDA stage. Interestingly, 12 percent or 25 percent of what comes through the IND-NDA stage is attributable to the preclinical stage. Thus, the amount of time lost by the pharmaceutical industry to regulatory requirements is four times more important from the IND to the NDA stage than it is at the preclinical stage. I emphasize that because I cannot possibly imagine how anyone could conclude on the basis of the data presented that the preclinical stage is significant and the regulatory stage of the IND and NDA is insignificant.

Let me turn now, Mr. Chairman, to my conclusion on page 49. PMA believes that, with the restored patent term for pharmaceutical products, the real cost of safe and effective therapy will not increase, and is likely to decrease. But for consumers the most important question is whether, absent patent restoration, the new therapy will exist at all. From the public viewpoint, the critical factor is not patent lives or research—it is safe and effective new medicine. And the erosion in NCE drugs parallels the erosion in patent life and research investment.

Turning to the top of page 51, the balance between innovation and price competition struck by Congress, to which you referred, Mr. Chairman, has been upset, and the public health is suffering as a result. We believe it is in the public interest to restore this balance. PMA therefore strongly supports the Patent-Term Restoration Act, which would again provide the incentive needed to invest in pharmaceutical innovation in this country.

The concept of patent-term restoration has been studied at length and in depth. All of the facts needed by Congress to resolve the matter have been made available and extensively reviewed. There has been one report and one analysis by the Office of Technology Assessment, and numerous congressional hearings to which you referred.

It is time for Congress to bring the matter to a decision. Those who oppose patent-term restoration legislation have continually asked for further information and further study. They want it studied to death. They want at all cost to avoid a resolution of the matter. We believe this is only a diversionary tactic. During a recent public interview, Secretary of Health and Human Services Schweiker was asked about doing a further study on patent-term restoration. He responded:

> I am not sure that is not a subterfuge that some people are using just to slow the whole process down. It seems to me it is a pretty simple, straightforward question. That either you have lost some time because of the drug approval process or you have not. I happen to believe we have.

PMA agrees with Secretary Schweiker. All of the pertinent facts and arguments have been identified, and the matter should be decided by Congress now.

Mr. Chairman, I thank you for your indulgence. This concludes my prepared statement, but I would be happy to answer the subcommittee's questions.

[The prepared statement of Peter Barton Hutt follows:]

Statement Of
Peter Barton Hutt
On Behalf Of The
Pharmaceutical Manufacturers Association
Before The
Subcommittee On Investigations And Oversight
Of The
Committee On Science And Technology
U.S. House Of Representatives

On

Drug Patent Term Restoration

February 4, 1982

Mr. Chairman and members of the Subcommittee, my name is Peter Barton Hutt. I am appearing today on behalf of the Pharmaceutical Manufacturers Association (PMA), which represents 140 companies that discover, develop, and produce prescription drugs and medical devices. PMA members introduce more than 90 percent of the new chemical entity (NCE) pharmaceuticals in the United States and a large portion of this country's medical device innovations as well.

PMA member companies are committed to improving health care by converting new scientific knowledge into safe and effective medicine for the benefit of all segments of the public. For that reason, we are pleased to testify today about the crucial role of patents in pharmaceutical innovation.

INNOVATION IN THE PHARMACEUTICAL INDUSTRY

A recent report of the National Academy of Sciences has defined "innovation" in the following way:

> "Economists define technological innovation as the initial commercial application of a new product or process. From the standpoint of the industrial firm, the activities leading to innovation involve a long-term investment decision process. This process incorporates the various stages of research, development, capital investment, and commercialization. A firm's investment in these activities are influenced by the same basic forces that govern outlays on other investment projects. Thus, investments for R&D and innovation will be determined by their perceived profits and risks relative to alternative investment opportunities as well as the cost and availability of funds for investment."[1]

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[1] National Academy of Sciences, The Impact of Regulation on Industrial Innovation 8 (1979).

In the pharmaceutical industry, innovation is thus best measured by the number of new chemical entity (NCE) drugs approved by the Food and Drug Administration (FDA) for marketing during any particular time. These NCE drugs represent, in the words of the National Academy, "the initial commercial application of a new product or process."

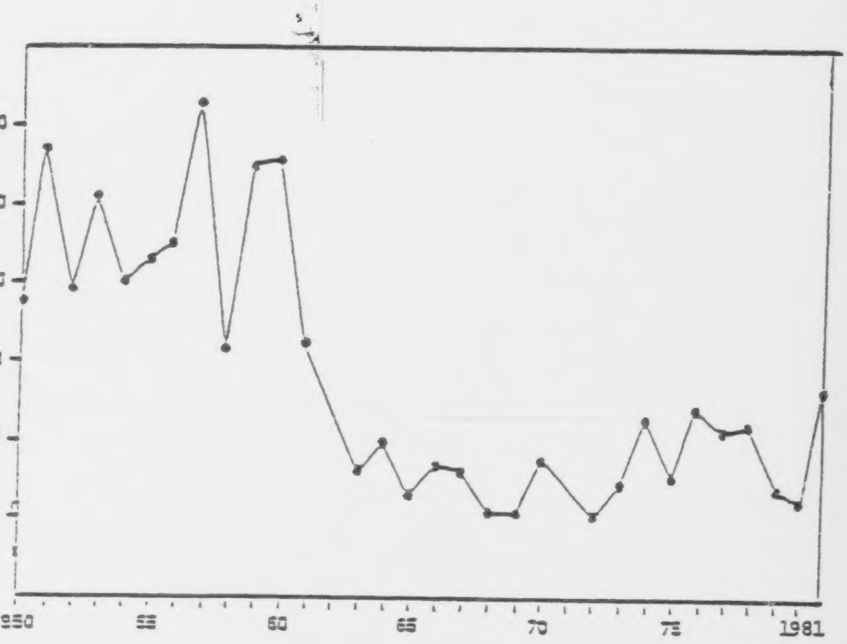
During the period from 1962 to the present, pharmaceutical innovation in the United States has declined substantially. Figure I shows the progressive and dramatic reduction in yearly FDA approvals of NCE drugs for use in this country. This reduction in pharmaceutical innovation is attributable to two interrelated factors.

First, drug research is lagging behind the growth rate of the drug industry. Pharmaceutical R&D expenditures continue at a fairly steady rate of 12 percent of drug sales. But when these figures are adjusted for inflation, it becomes apparent that the rate of pharmaceutical R&D in relation to drug sales has been reduced by about one-third in the past 15 years, because drug research costs have increased dramatically in relation to drug prices. This real decline in pharmaceutical R&D expenditures is shown in Figure II.

Second, the cost of developing and obtaining approval of an NCE drug has also risen dramatically. Regulatory requirements have increased. It is estimated that about 10,000 candidate drugs are synthesized for every one that actually gets to market. For every 10 drugs that reach the very expensive and time-consuming clinical investigation (IND) stage, only one is

Figure I

Number of New Chemicals Entities (NCEs)
Approved by FDA, 1950-1981[2]



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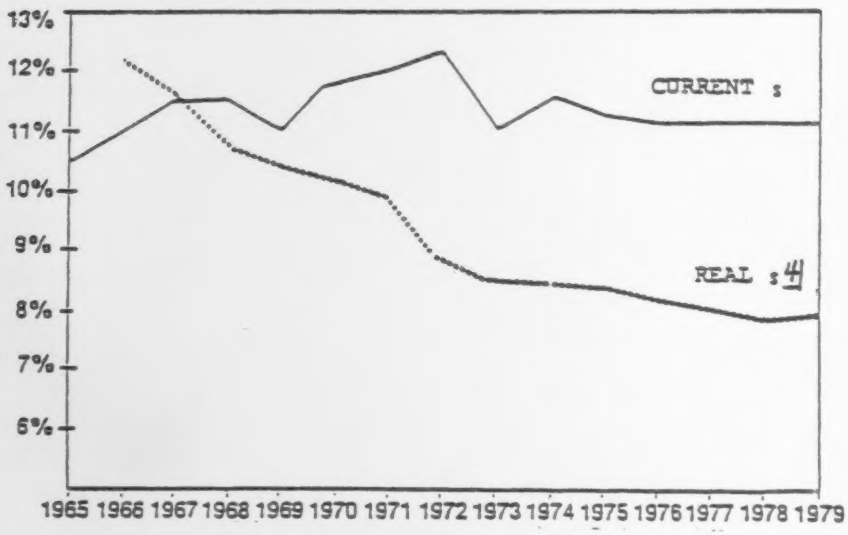
[2] "Health and the Environment: Miscellaneous -- Part 2, "Hearings before the Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives, 97th Cong., 1st Sess. 292 (1981); FDC Reports, January 11, 1982, p. 16.

Figure II

US Pharmaceutical R&D Expenditures

as a Percentage of U.S. Pharmaceutical

Sales, 1965-1979[3]



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[3] R&D as a percentage of sales is computed by dividing human and veterinary R&D expenditures in the United States by domestic production (i.e., domestic sales and exports, including subsidiaries abroad) times 100.

[4] Sales Deflator Producer Price Index for Ethical Pharmaceuticals, Bureau of Labor Statistics: 1967 = 100. R&D Deflator: Biomedical R&D deflator used by the National Institutes of Health, Department of Health, Education, and Welfare: 1967 = 100. PMA Annual Survey (various years).

ultimately marketed.[5] The cost of chemical, animal, and clinical testing of NCE drugs has soared. The time required for FDA approval is more than three times longer than it was 20 years ago. The cost of money has escalated. As a result, the total amount of investment needed to produce a single approved NCE drug, which has been estimated at about $6 million dollars in 1962 (or $16 million in 1980 dollars)[6] and increased to $54 million in 1976,[7] has now reached the almost unbelieveable level of $70 million.[8]

Thus, from any given level of R&D investment by the pharmaceutical industry today, the country realizes fewer NCE drugs than it once did. Coupled with a decrease in real R&D investment by the industry, it is not surprising that the statistics show a substantial decline in pharmaceutical innovation in the United States today.

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[5] Wardell, *The History of Drug Discovery, Development and Regulation*, in Chien, ed., *Issues in Pharmaceutical Economics* 10, 11 (1979).

[6] Bailey, *Research and Development Costs and Returns: The U.S. Pharmaceutical Industry*, 80 J. Pol. Econ. 78 (January/February 1972).

[7] Hansen, *The Pharmaceutical Development Process: Estimates of Development Costs and Times and the Effects of Proposed Regulatory Changes*, in Chien, ed., *Issues in Pharmaceutical Economics* 151 (1979).

[8] Calculated by PMA by applying to Hansen's 1976 estimate of $54 million the Biomedical R&D Deflator used by NIH to reflect inflation in R&D.

THE IMPORTANCE OF PHARMACEUTICAL INNOVATION

New chemical entity drugs represent our major hope, as a society, for reducing the burden of morbidity and mortality in this country. Pharmaceutical innovation is also a primary means through which the skyrocketing costs of health care can be brought under control and perhaps eventually even reduced.

The infectious diseases that took such a heavy toll at the turn of the century now cause less than two percent of the deaths they caused then.[9] Diseases dreaded as recently as 30 years ago now largely are under control. New pharmaceutical products have played a key role in the declining rates of death and disease shown in Table I and Table II for a wide variety of serious disease categories:

TABLE I

Decline in Death Rates[10]

(per 100,000 in specified group)

	1960	1980	% Change
Measles	380	10	-97.4
Meningitis	2,316	1,320	-43.0
Rheumatic Fever and Rheumatic Heart Disease	18,411	7,950	-56.8
Streptococcal Sore Throat, Scarlatina, and Erysipelas	108	10	-90.7

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[9] Fries, Aging, Natural Death, and the Compression of Morbidity, 303 N. Eng. J. Med. 130, 132 (1980).

[10] National Center for Health Statistics, Monthly Vital Statistics Report -- Annual Summary of Births, Deaths, Marriages

(footnote cont'd)

	1960	1980	% Change
Syphilis	2,945	180	-93.9
Tuberculosis	10,866	1,770	-83.7
Ulcer of Stomach and Duodenum	10,830	5,750	-46.9
Whooping Cough	120	10	-91.7

TABLE II

Decline in Disease Rates[11]

	1960	1970	1980	% Change
Measles	441,703		13,506	-96.9
Mumps		104,953	8,576	-91.8
Rheumatic Fever, Acute	9,022		432	-95.2
Rubella		56,552	3,904	-93.1
Tuberculosis	55,494		27,749	-49.9
Whooping Cough	14,809		1,730	-88.3

(footnote cont'd)

and Divorce: United States, 1980, Vol. 29, No. 13, p. 20 (September 17, 1981); National Center for Health Statistics, *Vital Statistics of the United States, 1960*, Vol 2, Pt. A., p. 5-102 (1961). The death rate for mumps declined 93.0 percent during 1968-1978; for acute rheumatic fever declined 81.2 percent during 1960-1978; and for rubella declined 58.3 percent during 1968-1978. *Id*.

[11] U.S. Department of Health and Human Services, *Morbidity and Mortality Weekly Report -- Annual Summary, 1981*, Vol. 29, No. 56, pp. 12 & 14 (September 1981); *Morbidity and Mortality Weekly Report -- Annual Supplement, 1961*, Vol. 29, No. 54, p. 4 (September 1961).

Medicine to achieve the same dramatic results against our current leading causes of death, heart disease and cancer are now major targets for the pharmaceutical industry.

It is not true that only major new "breakthrough" drugs contribute to this reduction in morbidity and mortality. We must pursue progress in small, as well as large, increments. A new drug is not uniformly safe and effective throughout the entire population. Biological variations among people require development of a large armamentarium of drugs to assure that the benefits of pharmaceutical science reach as many as possible.

development of a number of new drugs which, although not broadly classified as "breakthrough" products for society as a whole, are nonetheless of crucial importance to individual patients for the alleviation and cure of their disease. That is why the availability of a wide variety of drugs for any particular disease is so vital to the public health.

Drug prices have been one component of health care costs that has remained relatively stable over the last 20 years. While the consumer price index has risen 178 percent and health care costs have increased 629 percent, the cost of prescription drugs has increased only 34 percent.[12] As shown in Table III, the drug share of national health expenditures has declined every year during this past decade:

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[12] U.S. Department of Labor, Bureau of Labor Statistics, CPI Reports, (various issues); U.S. Department of Health and Human Services, Health Care Financing Administration, Health Care Financing Review, (various issues).

TABLE III

DRUG SHARE OF NATIONAL HEALTH EXPENDITURES[13]

(in billions of dollars)

Year	Total National Health Expenditures	Drugs & Medical Sundries[14]	Drugs & Drug Sundries % of Total
1970	74.7	8.0	10.7
1971	83.3	8.6	10.3
1972	93.5	9.3	10.0
1973	103.2	10.1	9.7
1974	116.4	11.0	9.5
1975	132.7	11.9	9.0
1976	149.7	13.0	8.7
1977	169.2	14.1	8.3
1978	189.3	15.4	8.1
1979	214.6	17.2	8.0
1980	247.2	19.2	7.8

The continual introduction of new drugs thus not only can improve therapy, but at the same time can help keep down the price of all medicine and make drug therapy more cost-effective.

In an era when the cost of Medicare and Medicaid threatens the stability of our entire economy, one need only look at the savings from new drug introductions to appreciate how better therapy can produce lower costs. Tagamet, Smith-Kline's new ulcer drug -- if used by all those who could benefit from it -- could save some $250 million a year in foregone surgery and physician visits.[15] Antipsychotic medicine for the control of mental illness has shortened treatment periods and reduced the need for expensive hospitalization. In 1973, only 35 percent of mental illness patients required inpatient service, down from 77 percent in 1955.[16]

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[13] "National Health Expenditure 1980," Health Care Financing Review, September 1981, p. 32.

[14] Prescription drugs are 57 percent of this total. Id. at 10.

Pharmaceutical innovation thus saves lives, improves the quality of life, and reduces the cost of health care -- all at the same time.

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[15] Robinson Associates, Inc., The Impact of Cimetidine on the National Cost of Duodenal Ulcers (1978).

[16] Statistical Abstract of the United States 83 (1975).

The importance of patent protection obviously increases with the size of the investment needed to achieve innovation in any field. If innovation can be purchased cheaply, patent protection is relatively unimportant. As the investment cost escalates, however, patent protection becomes far more important. In the pharmaceutical industry, where the cost of an NCE has escalated so dramatically, the assurance of strong patent protection has become increasingly crucial to the future of the industry.

This fact was explicitly recognized in the recent report by the Office of Technology Assessment on patent term restoration:

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[17] Dawson Chemical Co. v. Rohm & Haas Co., 448 U.S. 176, 221 (1979).

[18] Markey, Technology's Children, 7 (February 9, 1981).

> " . . .once a drug has been discovered, developed, and marketed by a firm, other firms can produce and sell the drug at a price that is considerably lower than that of the innovator since their price need not include the cost of research and development (R&D) or the cost of creating a market. Thus, if there are no restrictions on market entry, later entrants may have a significant competitive advantage.
>
> In view of these facts, research intensive pharmaceutical firms consider patent protection as a prerequisite to innovation."[19]

A General Accounting Office report found in 1968 that pharmaceutical companies would not invest resources in screening new chemicals for medical usefulness unless the companies could obtain the patent rights to the compounds involved.[20] In 1980, Congress enacted legislation granting to private enterpise patents on inventions conceived with government funds because those inventions otherwise might never be commercialized.[21] Without an adequate patent system, innovation in the pharmaceutical industry would wither and the public health would correspondingly suffer.

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[19] Office of Technology Assessment, Patent-Term Extension and the Pharmaceutical Industry 49 (1981) (cited hereafter as the "OTA Report").

[20] GAO, Problem Areas Affecting Usefulness of Results of Government-Sponsored Research in Medicinal Chemistry, Rep. No. B-164031(2), at 18-9 (1968).

[21] P.L. 96-517, 94 Stat. 3015, 3019 (1980).

In 1861, Congress selected 17 years as the period of patent exclusivity.[22] Since 1861, the 17-year patent year term has remained unchanged.

No one can prove empirically that 17 years was then, or is now, the perfect patent term. But no one can deny that the patent system, as it has existed for more than 100 years, has contributed enormously to innovation generally, and to pharmaceutical innovation in particular.

THE DRUG RESEARCH, INVESTIGATION, AND APPROVAL PROCESS

The report prepared in 1980 by the House Subcommittee on Science, Research, and Technology demonstrates the major impact of FDA regulatory requirements throughout the drug development process -- from the moment a new chemical entity is synthesized until final FDA approval of a new drug application (NDA).[23] That process is divided into three major stages: preclinical research, clinical investigation, and NDA approval.

Preclinical Research. Before clinical investigation of a new chemical entity may begin, substantial research must be undertaken on the chemical, pharmacologic, and toxicologic properties of the chemical in order to meet FDA prerequisites for clinical research. As the report of the House Subcommittee states, the FDA requirements:

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[22] 12 Stat. 246, 249 (1861).

[23] "The Food and Drug Administration's Process for Approving New Drugs," Report prepared by the Subcommittee on Science, Research and Technology, Committee on Science and Technology, House of Representatives, 96th Cong., 2d Sess. (1980).

> ". . . affect the type and direction of research and other development activities which must be done once a new chemical entity is identified."[24]

The FDA investigational new drug (IND) regulations require that such preclinical research include sufficient chemical information about the drug to set exact specifications, using sophisticated analytical methodology, to assure little or no variation in the entity. An IND must contain:

> "A statement of the methods, facilities, and controls used for the manufacturing, processing, and packing of the new drug to establish and maintain appropriate standards of identity, strength, quality, and purity as needed for safety and to give significance to clinical investigations made with the drug."[25]

Such preclinical research can be enormously costly and time-consuming.[26]

The IND regulations also require that, before clinical investigation may begin, sufficient animal testing data must exist to justify use of the chemical in humans. An IND must contain:

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[24] *Id.* at 13-14. FDA has stated that preclinical and clinical testing "is subject to a comprehensive regulatory scheme." 46 Fed. Reg. 34093 (June 30, 1981).

[25] Item 5, FDA Form FD-1571, 21 C.F.R. 312.1(a)(2).

[26] A recent FDA report has disclosed that 60 percent of the deficiencies cited by FDA during the NDA review process relate to such chemical and manufacturing information. FDA, *Approvals and Non-Approvals of New Drug Applications During the 1970s*, OPE Study 57, at v (1980).

> "Adequate information about the preclinical investigations, including studies made on laboratory animals, on the basis of which the sponsor has concluded that it is reasonably safe to initiate clinical investigation with the drug: such information should include identification of the person who conducted each investigation; identification and qualifications of the individual who evaluated the results and concluded that it is reasonably safe to initiate clinical investigations with the drug and a statement of where the investigations were conducted and where the records are available for inspection; and enough details about the investigations to permit scientific review. The preclinical investigations shall not be considered adequate to justify clinical testing unless they give proper attention to the conditions of the proposed clinical testing. When this information . . .indicates a need for full review of the preclinical data before a clinical trial is undertaken, the department will notify the sponsor to submit the complete preclinical data and to withhold clinical trials until the review is completed and the sponsor notified."[27]

FDA has established both formal[28] and informal[29] guidelines that can include extensive animal testing before an IND can be submitted. The FDA requirements for good laboratory practices (GLP) in conducting preclinical research for a new drug have substantially added to both the cost and the time for this type of research.[30]

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[27] Item 6(a), FDA Form FD-1571, 21 C.F.R. 312.1(a)(2).

[28] Formal guidelines are issued by FDA pursuant to 21 C.F.R. 10.90(b). E.g., 44 Fed. Reg. 20796 (April 6, 1979); 45 Fed. Reg. 41705 (June 20, 1980); 46 Fed. Reg. 24693 (May 1, 1981).

[29] E.g., D'Aguanno, Drug Toxicity Evaluation -- Pre-Clinical Aspects and Guidelines for Reproduction Studies for Safety Evaluation of Drugs for Human Use, in FDA Introduction to Total Drug Quality, DHEW Pub. No. (FDA) 74-3006), at 35, 41 (1973).

[30] 21 C.F.R. pt. 58; 41 Fed. Reg. 51206 (November 19, 1976); 43 Fed. Reg. 59986 (December 22, 1978).

Accordingly, it is not surprising that the House Subcommittee report found that preclinical research can take 1-4 years to complete.

Clinical Investigation. Once adequate preclinical research is completed, an IND can be filed to justify clinical investigation of the new chemical entity in humans. The amount of information required by FDA to be filed with an IND is extensive. The IND regulations, including the requirements for protection of human subjects, currently comprise some 25 pages in the Code of Federal Regulations.

Just as the IND provisions impose regulatory requirements on preclinical research, the NDA provisions impose regulatory requirements on the clinical investigation conducted pursuant to an IND. Lengthy and detailed FDA regulations and guidelines establish what the Agency demands in the nature of evidence of safety and effectiveness for a new drug. It is well-known that these requirements are rigorous and demanding. They exceed what is required in other countries.[11] The time spent on clinical investigation has therefore increased dramatically, as shown in Figure III. The House Subcommittee report found that it takes about 4-6 years to conduct this IND research in accordance with FDA requirements.

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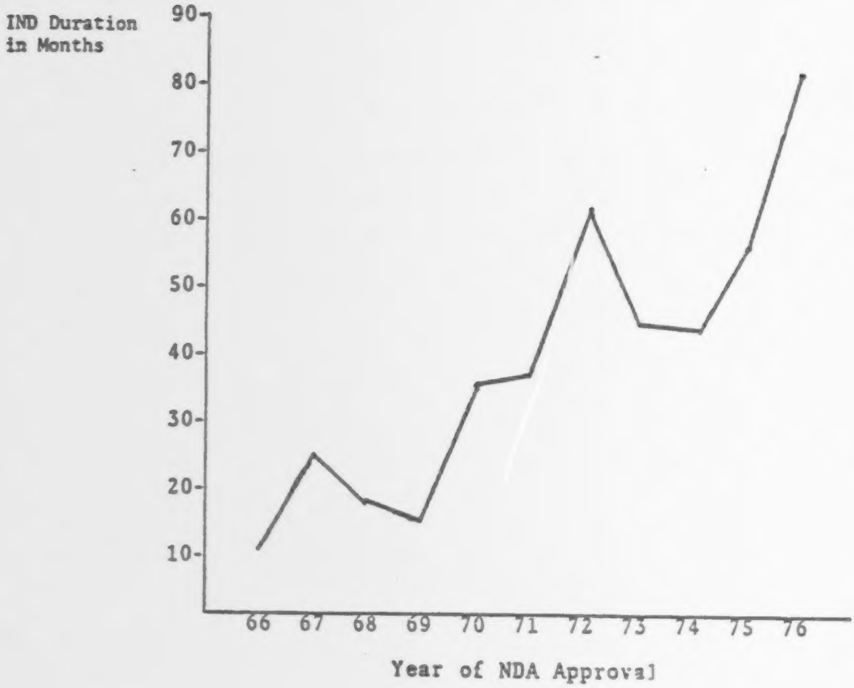
[11] General Accounting Office, FDA Drug Approval -- A Lengthy Process that Delays the Availability of Important New Drugs, Rep. No. HRD-80-64 (1980).

Figure III

Trends in IND Duration[12]



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[12] Wardell, DiRaddo, & Trimble, Development of New Drugs Originated and Acquired by United States-Owned Pharmaceutical Firms, 1963-1976, 28 Clin. Pharmacol. & Therap. 272 (1980). IND duration is defined as the mean time from IND filing to NDA submission.

NDA Approval. After the FDA requirements for preclinical research and clinical investigation are completed, an NDA is submitted to the Agency to obtain approval of the drug for marketing. Until that approval is obtained, the drug may not be commercialized.

The statute requires FDA to act upon an NDA within 6 months. The House Subcommittee report found that the average NDA approval time was 14 months in 1963, rose to 37.3 months in 1971, dipped to 20.0 months in 1976, and climbed back up to 35.2 months in 1979. The vast majority of these NDAs are eventually approved, but the amount of time taken by FDA to review them, during which the drugs cannot be marketed, is very significant.

Attempts at Improvement. During the past few years, numerous studies have been conducted to determine how the regulatory process governing new drugs could be improved. While all of these studies offer suggestions for improvement, none is optimistic that such improvement will be substantial. Dr. Crout, Director of the FDA Bureau of Drugs, summed it up by stating that:

> "While it would not be easy, I believe there are some opportunities to reduce this time in the future -- but, in my judgment, not more than a year or so -- by modification of certain regulatory requirements and by continuing our emphasis on efficient management of the review process."[14]

THE GRADUAL EROSION OF PHARMACEUTICAL PATENT PROTECTION

Although Congress has not changed the 17-year patent term for pharmaceutical products, the government research, testing, and approval requirements just described have substantially reduced the effective length of that term.

When a drug firm discovers a promising new chemical compound, the first thing it does, even before making the investment to develop it into a marketable medicine, is to file for a patent. Once that patent is issued, its 17-year term immediately begins to run. But at the time the patent is issued, the innovating firm may be far from sure it will ever have a marketable drug. For that assurance the government requires substantial chemical, animal, and human testing and then FDA approval of a new drug application (NDA) for the product. This testing and approval usually takes about 7-13 years.[18]

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[14] "Health and the Environment: Miscellaneous -- Part 2," Hearings before the Subcommittee on Health and Environment, Committee on Energy and Commerce, House of Representatives, 97th Cong. 1st Sess. 279 (1981) (emphasis added).

For pharmaceutical products, therefore, the 17-year patent term has become a legislative figment. In reality, a drug patent has a much shorter effective life. As a result, incentives to invest in pharmaceutical R&D have been substantially reduced.

The erosion of effective patent life for pharmaceuticals began about 20 years ago. It coincides with the erosion in pharmaceutical innovation, as measured by the yearly FDA approval of NCE drugs.

It is readily apparent that the public has been the loser. The sick, and particularly the elderly -- the people with diseases for which medicine has not yet been developed -- have been the real victims of lost patent life and reduced pharmaceutical innovation.

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[18] "The Food and Drug Administration's Process for Approving New Drugs," Report of the Subcommittee on Science, Research and Technology of the Committee on Science and Technology, House of Representatives, 96th Cong. 2d Sess. 13 (1980).

STUDIES ON EFFECTIVE PATENT LIFE OF NCE DRUGS

A number of studies have been conducted, each using a somewhat different methodology and data base, to study the precise reduction that has occurred in the effective patent life for NCE pharmaceutical products during the past 20 years. In response to a request by this Subcommittee, PMA has itself conducted a review of the effective patent life of NCE drugs approved by FDA during 1980.

All studies show the same trend. Both individually and in combination, they confirm a substantial decrease in effective drug patent terms. The effective patent life of the NCE drugs approved by FDA in 1980 was less than half the 17 years provided by Congress.

Pracon Study. A study conducted by Pracon, Inc., an independent consulting firm, for Hoffmann-La Roche, Inc., found that the average effective patent life of NCE drugs approved by FDA during 1950-1977 was reduced from 18.2 years to 8.8 years.[16]

The Schwartzman Study. Professor David Schwartzman of the New School for Social Research in New York City studied the NCE drugs approved by FDA during 1966-1973.[17] He calculated the arithmetic mean of the effective patent life of NCEs during this time to be 13.1 years. Moreover, he found a progressive reduction in the effective patent life during that period, from 13.9 years in 1966-1973 to 12.4 years in 1970-1973.

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[16] Pracon, Inc., The Effective Patent Life of Pharmaceutical Products: Trends and Implications (1978).

[17] Schwartzman, Innovation in the Pharmaceutical Industry 167-173 (1976).

The Statman Study. Professor Meir Statman of the University of Santa Clara studied a sample of 126 NCE drugs approved by FDA during 1949-1975.[38] He found "a continuous decline in the effective life of drug patents" and developed an equation to estimate the effective life of drug patents for 1960-1978.

The Eisman and Wardell Study. Professors Martin Eisman and William Wardell of the University of Rochester studied the effective life of NCE drug patents during 1966-1979.[39] They found the effective patent life declined from 13.6 years in 1966 to 9.5 years in 1979.

The PMA Study. At the request of the Subcommittee, PMA has obtained additional data for the year 1980. These data are set out in Table IV. They show that, for NCE drugs approved by FDA in 1980, the effective patent life has decreased still further, to 7.4 years.

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[38] Statman, *The Effect of Patent Exporation On The Market Position of Drugs*, in Helms, *Drugs & Health: Economic Issues & Policy Objectives* 140 (1981); and in *Managerial and Decision Economics*, June 1981, p. 61.

[39] Eisman & Wardell, *The Decline in Effective Patent Life of New Drugs*, *Research Management*, January 1981, p. 18.

TABLE IV

PATENTS FOR DRUGS APPROVED BY FDA IN 1980

TRADE NAME	GENERIC NAME	COMPANY OBTAINING NDA	PATENT NUMBER	TYPE OF PATENT	DATE PATENT FILED	DATE PATENT ISSUED	DATE OF FDA APPROVAL	EFFECTIVE PATENT LIFE
Viroptic	trifluridine	Burroughs-Welcome	3201387	Compound	9/18/63	8/17/65	4/10/80	2 years - 4 months
Meclan	meclocycline	Johnson & Johnson	2984686	Compound	12/19/60	5/16/61	5/30/80	none
Cinobac	cinoxacin	Lilly	3669965	Compound	2/4/69	6/13/72	6/13/80	9 years - 0 months
Meclomen	meclofenamate sodium	Parke Davis	3313848	Compound	1/12/61	4/11/67	6/25/80	3 years - 10 months
Vansil	oxamniquine	Pfizer	3821228	Compound	5/29/68	6/28/74	7/23/80	10 years - 11 months
			3903283	Use 40/	4/19/74	9/2/75	7/23/80	12 years - 2 months
Calderol	calcifediol	Upjohn	3833622	Compound 41/ (hydrate form)	3/17/69	9/3/74	8/5/80	11 years - 1 month
			4004003	Use	10/6/75	1/18/77		
Yutopar	ritodrine hydrochloride	Merrell-Dow	3410944	Compound & Composition	2/25/65	11/12/68	8/29/80	5 years - 3 months

40/ Divisional requirement imposed on patent applicant by Patent Office

41/ There is an earlier issued compound patent (patent issued date 2/23/71) owned by another party under which Upjohn is licensed. If effective patent life were calculated from this earlier issued patent the effective patent life for calcifedlol would be 7 years, 6 months.

PATENTS FOR DRUGS APPROVED BY FDA IN 1980

TRADE NAME	GENERIC NAME	COMPANY OBTAINING NDA	PATENT NUMBER	TYPE OF PATENT	DATE PATENT FILED	DATE PATENT ISSUED	DATE OF FDA APPROVAL	EFFECTIVE PATENT LIFE
Asendin	amoxapine	Lederle	3681357	Compound[42] (selection patent)	2/28/64	8/1/72	9/22/80	8 years - 11 months
			3663696	Use	2/28/64	5/16/72	9/22/80	8 years - 8 months
Zomax	zomepirac sodium	Johnson & Johnson	3752826	Compound	7/26/67	8/14/73	10/28/80	9 years - 10 months
			4070368	Process	6/17/74	1/24/78	unknown	
			4213905	Process	6/25/79	7/22/80	unknown	
Siseptin	sisomicin sulfate	Schering-Plough	3907771	Compound	6/27/78	9/23/75	10/29/80	11 years - 11 months
			3832286	Process[43]	6/27/78	8/27/74	unknown	
Ludiomil	maprotiline hydrochloride	Ciba-Geigy	3399201	Compound	11/9/61	8/27/68	12/1/80	4 years - 8 months
Spectrobid	bacampicillin hydrochloride	Pfizer	3873521	Compound	9/7/71	3/25/75	12/22/80	11 years - 3 months
			3939270	Composition[44]	3/8/73	2/17/76	12/22/80	12 years - 2 months

[42] For amoxapine there is an earlier compound patent (issue date 12/8/70) covering the generic class of compounds, owned by another party, under which Lederle is licensed. If effective patent life were calculated from this earlier issued patent, the effective patent life for amoxapine would be 7 years, 3 months.

[43] Divisional requirement imposed on patent applicant by Patent Office.

[44] Divisional requirement imposed on patent applicant by Patent office.

All Studies Combined. In order graphically to illustrate the results of these studies, we have plotted them on the chart shown in Figure IV. The congruence of these studies is striking.

THE ROLE OF COMPOUND, COMPOSITION, USE, AND PROCESS PATENTS

The recent Office of Technology Assessment report contains a very helpful description of pharmaceutical patents.[48] To summarize, under existing law every patent application -- whether for a pharmaceutical product or for some other invention -- must disclose the product, a method of using the product, and a process for making the product. (For a drug patent, the product itself may be described as either a single chemical compound or group of compounds or as a composition of chemicals.) All patent applications must then specify which aspects of the disclosed information are claimed as part of the invention. Only those aspects claimed as the invention can be patented.

It is important to understand that the initial compound or composition patent application for a new pharmaceutical must, like any other patent application, disclose a use for the product and a method for making the product. On occasion, in the past, the Patent and Trademark Office has required that the claims in a patent application respecting methods of use or process be split off from the compound claims and submitted in so-called "divisional applications."

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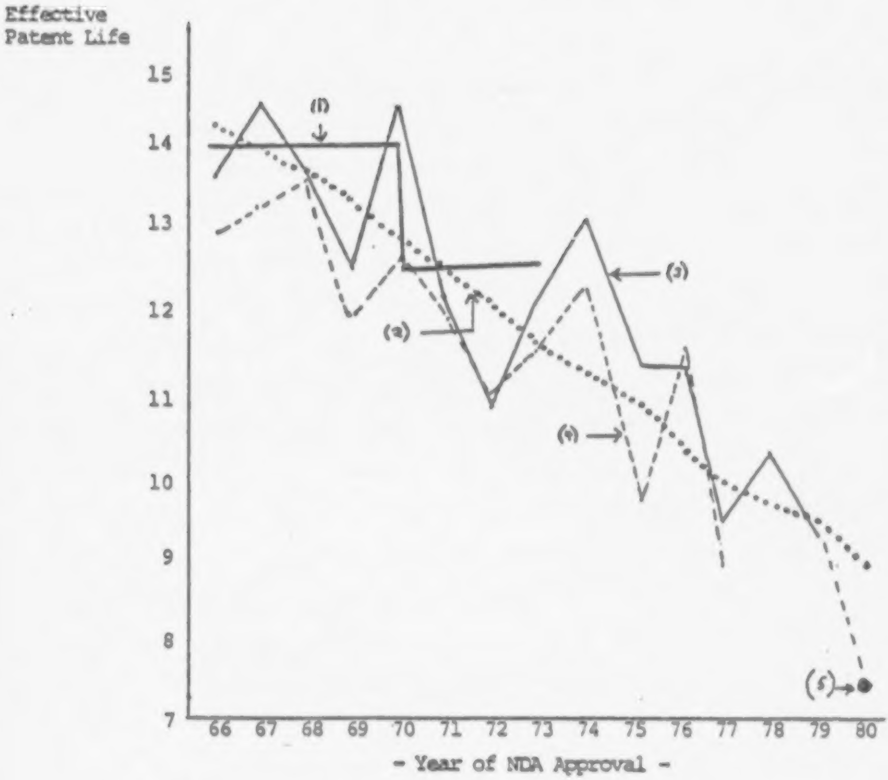
[48] OTA Report 50-52.

Figure IV

TRENDS IN EFFECTIVE PATENT LIFE (EPL) FROM VARIOUS SOURCES



(1) Schwartzman.

(2) Statman.

(3) Eisman & Wardell.

(4) Pracon.

(5) PMA.

As of a few years ago, however, the Patent and Trademark Office largely discontinued this practice.

Once a patent application is filed or granted -- whether for a pharmaceutical product or for some other invention -- additional patent applications may also be filed to cover related new inventions. For example, an entirely new use may be found for a product that had not been described before, or a new process may be found to make the product more cheaply, or with fewer impurities, or in some other useful way.

These subsequent patents, including use patents and process patents, are also important to innovation. Companies must invest substantial resources to develop new uses for, and methods of manufacturing, existing products. Without the incentives provided by the patent system, these investments surely would be less attractive and perhaps would never be made at all.

In 1972, FDA issued a proposed policy statement expressing concern about unapproved uses of approved new drugs.[47] FDA urged physicians and manufacturers to cooperate in obtaining the data necessary to substantiate such uses. Without the possibility of a use patent, there would be no incentive for any company to expend the resources necessary for such an effort.

New processes can be equally important. Not infrequently they will produce a product that is safer or more effective, through reduction of impurities, increased stability, or other important attributes. Of equal significance, new processes may well result in substantially lower manufacturing costs, thus permitting the company to hold the line on, or even reduce, prices to the consumer even in the face of major inflationary pressures. Process patents have undoubtedly contributed to the superb record of the pharmaceutical industry in holding down price increases during the past 20 years.

THE PATENT TERM RESTORATION ACT

Legislation designed to restore, at least in part, the effective patent life originally intended by Congress, is

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[46] *Dawson Chemical Co.* v. *Rohm Haas Co.*, 448 U.S. 176, 221-222 (1979)(footnotes omitted).

[47] 37 Fed. Reg. 16503 (August 15, 1972).

now being considered in Congress. This legislation has been passed by the Senate.[48] It has been the subject of hearings before the Subcommittee on Courts, Civil Liberties, and the Administration of Justice of the House Committee on the Judiciary and is now awaiting markup there. PMA strongly supports this legislation and urges its enactment as quickly as possible.

The Patent Term Restoration Act would restore to patent owners up to seven years of the patent life lost to government premarket research, testing, and approval requirements. Although not limited to any particular class of products, the bill would have the greatest impact on those products, such as drugs, which are subject to the most rigorous and time-consuming regulatory requirements.

Upon application to the Patent and Trademark Office, the owner of a patent subject to one of the regulatory review periods specified in the bill would receive a limited extension of the patent term. For a new drug, the extension would generally equal the time from the investigational new drug (IND) filing with FDA to approval of the new drug application (NDA), but no more than a maximum of seven years. If the patent is granted after the IND is submitted but before the NDA is approved, the extension would be measured from the date of the patent to the date of the NDA approval. If the patent is granted after the NDA is approved, there would be no patent term extension. Accordingly, no patent could be extended beyond the statutory 17 years.

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[48] 127 Cong. Rec. S7356 (July 9, 1981) (daily ed.); S. Rep. No. 97-138, 97th Cong., 1st Sess. (1981).

The bill provides a new climate of restored incentives for pharmaceutical innovation. It is justified on grounds of both fundamental equity and protection of the public health.

First, it is plainly inequitable for an NCE drug, once approved by FDA, to have only an average patent life of 7.4 years, when other inventions can obtain an effective patent life of 17 years. This is not a question of industry asking for special treatment. The bill is designed simply to provide for drugs the same consideration Congress has given to other inventions.

Even if the Patent Term Restoration Act is enacted into law, drug patents will continue at a disadvantage. As noted, the legislation allows a maximum of only seven years patent extension. Thus, if it were applied to the NCE drugs approved by FDA during 1980, it would have increased the average effective patent life to 14.4 years, but ⑮ would not have fully restored the 17 years intended by Congress.

The legislation provides no windfall for the pharmaceutical industry. It merely provides some, but not all, of what has been lost as a result of increased governmental research, testing, and approval requirements during the past 20 years. On the basis of equity alone, the legislation is fully justified.

Second, this legislation is vitally needed to re-invigorate pharmaceutical investment and thus to help return pharmaceutical innovation to its former stature. The public interest is best served when new therapies that are safe and effective become available as quickly as possible. For this to happen, incentives to invest in pharmaceutical research and development must be adequate. The current downward trend in real R&D investment in the pharmaceutical industry and in pharmaceutical innovation can only be halted, and hopefully reversed, if the industry perceives that a major change in policy has provided new incentives.

Investment decisions are not made on the basis merely of mathematical computations. Intangible factors, such as the perception of business managers about current governmental and public attitudes toward the industry, play an important role. During the past 20 years pharmaceutical executives have perceived an increasing indifference toward the drug industry, indicated by substantially more burdensome governmental requirements and the decrease in effective patent life. In such an atmosphere, it is not surprising that investment and innovation have declined. They will continue to decline if this atmosphere prevails.

One part of turning this around -- and we believe an important part -- is the Patent Term Restoration Act. It will signal a return to public encouragement of the development of important new pharmaceutical agents. Another part is the current review of FDA regulatory requirements for new drugs. PMA strongly supports the current efforts of the Commission on the Federal Drug Approval Process sponsored by Congressman Gore and the IND/NDA review by FDA to revise the new drug review system to reduce the time required for governmental approval. It is apparent, however, that this alone will not solve the problem of devalued patents for pharmaceutical products. Even if the time to NDA approval were reduced by a year, the effective patent life for new drugs would still be less than 10 years.

One cannot prove with mathematical precision that the Patent Term Restoration Act or the IND/NDA revision effort will in fact result in a specific number of new drugs becoming available that otherwise would be lost to our society. But the chief executives and the research directors of PMA member companies believe that these efforts, if they succeed, will be a major stimulus to new research.

GPIA ARGUMENTS

Critics of the Patent Term Restoration Act, led by the Generic Pharmaceutical Industry Association (GPIA), cite two principal arguments. First, they contend it will result in higher drug prices during the period that the patent is extended. Second, they contend that the industry is already able to protect its inventions through multiple use and process patents and thus that further legislation is unnecessary. Neither of these arguments is valid.

The development of new drugs, and new methods of using and making older drugs, represents the single greatest hope of this country for holding down health care costs. If one eliminated the new drugs developed in this country during the past 20 years, the cost of health care would have increased far more than it has. Particularly for the elderly and the poor, the development of safe and effective new drugs is essential to assure that all segments of our population receive adequate medical treatment at a reasonable cost.

Moreover, increased incentives for innovation will result in a higher level of pharmaceutical research, development of a larger number of drugs, and thus the marketing of drugs to compete with important existing drugs in order to provide price competition. This is not mere economic theory. The major new antiulcer drug, Tagamet, for example, was on the market only four years before a competitor, Carafate, appeared.[49]

Nor can the industry continually protect a product from competition once the basic compound or composition patent has expired. As already explained, that patent must disclose the compound or composition, a method of use, and a method of manufacturing. Once the patent expires, any competitor is

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[49] FDC Reports, September 28, 1981, p. 7 and November 9, 1981, p. 6.

free to market that compound or composition, made in the way disclosed in that patent, for any use disclosed in that patent.[58]

To the extent that the original patent holder makes further investments resulting in new inventions relating to that compound or composition, for which additional patents are in fact granted, those specific new uses and processes would remain the exclusive property of the patent holder for the length of the patent period that covers them. *Those new patents could not, however, prevent a competitor from making the product and marketing it in accordance with the specifications and for the uses disclosed in the original expired compound or composition patent*.

The attack made upon subsequent use and process patents is an ill-disguised attack upon the basic patent system itself. In substance, these attacks contend that the research-intensive pharmaceutical companies either must be content with an effective patent life that is half that granted by Congress to all other industries, or must forego any incentive whatever for developing new uses and new methods of manufacture for existing products. This approach would be counter-productive and self-defeating. It would single out pharmaceutical products for discriminatory and indeed punitive treatment. It would destroy incentive to develop and improve life-saving drugs. It rests solely upon the short-term hope of immediate reduced prices for a few drugs, brought about by competition from generic drug manufacturers, and sacrifices the long-term economic health of the pharmaceutical industry and the public health of the country as a whole. We strongly urge that this short-sighted approach, which would seriously endanger the future of innovation in the pharmaceutical industry, be rejected.

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[58] *OTA Report* 52.

In congressional testimony, the GPIA has rested its case primarily upon one table, listing 12 important drugs, which purports to show that the effective patent protection averages 18.5 years.[51] For a number of reasons, that table offers no persuasive argument against patent restoration. Indeed, properly analyzed, it strongly supports the PMA position.

First, contrary to the GPIA description of that table, it does not list "the most frequently prescribed drugs in America." Those drugs were selected, from a list of drugs with high dollar sales volume, in order to demonstrate lengthy patent protection.[52] Other drugs, with greater sales, could be selected to show a much shorter length of patent protection.

Second, the NDAs for eight of those 12 drugs were approved prior to 1968. The latest NDA of the 12 was approved in 1978. In those earlier years, the effective patent life was of course longer than it is today. In short, the GPIA table does not address the central issue -- that the effective patent life today, on an average is less than eight years.

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[51] Statement of Kenneth N. Larsen, Chairman of GPIA, before the Subcommittee on Courts, Civil Liberties, and the Administration of Justice, House of Representatives 5 (October 1, 1981).

[52] The drugs with the two longest effective patent lives shown were ranked 39th and 57th on the list of frequently prescribed drugs, and were prescribed less frequently and had a smaller dollar sales volume than other drugs with half their effective patent life.

Third, the same decrease in effective patent life is shown by the GPIA table as by the studies plotted in Figure III of this statement. The drugs approved prior to 1968 show longer effective patent lives. The drugs approved in 1976-1978 show shorter effective patent lives, demonstrating the effect of increased regulatory requirements.

Fourth, had the bill been enacted into law when those 12 drugs were first marketed, it would have provided no patent restoration for seven of the 12 listed drugs, only one year of patent restoration for three of the drugs, and four and six years for the remaining two. That is because the bill only restores patent protection where it has been lost as a result of the regulatory process. If no protection is lost, nothing is restored. If the NDA is approved before the patent is granted, there would be no patent term extension regardless of the extensive regulatory requirements. In short, the very equity that has been destroyed under existing law would be guaranteed under the new legislation. There could be no possibility of increasing patent protection beyond the statutory 17 years.

THE OFFICE OF TECHNOLOGY ASSESSMENT REPORT

The recent OTA report on Patent-Term Extension and the Pharmaceutical Industries provides support for the enactment of the Patent Term Restoration Act. It deals specifically with the likely effects of the legislation or pharmaceutical research and development, generic firms, and consumers.

R&D. The OTA report makes the following important findings:

> "The costs of R&D for the average new chemical entity drug have increased." (p. 4)
>
> "Since 1966, average effective patent terms have declined . . ." (p. 4)
>
> "Patent term extension will enhance the incentives provided by patents for pharmaceutical research and development." (p. 45)
>
> "On balance, there is a reasonable likelihood that firms may undertake or increase pharmaceutical R&D activities because of the increased incentives provided by the longer effective patent term." (p. 40).

Although OTA could not quantify the effect of patent term restoration on innovation, an increase in pharmaceutical R&D activities should result in a higher return in the form of an increased number of NCE drugs approved by FDA.

Generic Firms. The OTA report suggests that, in the long run, "production-intensive firms" (generic drug firms) as well as "research-intensive firms" should benefit if innovation increases because there will be more pharmaceutical products to market. The report makes the basic point that, although "patent-term extension delays their [generic firms'] entry into the market," the generic firms "must rely on research-intensive firms as sources of new products." (p. 44) If new drugs are not developed, no companies will be able to manufacture and sell them.

Consumers. Finally, the Report states that:

> "Consumers will benefit [from patent-term restoration] if more and better pharmaceuticals are developed. These pharmaceuticals can provide substantial savings over other forms of health care." (p. 7)

The report is unable to determine the precise effect on consumer expenditures for drugs or on the total cost of health care in the United States because of the offsetting effects of higher prices for drugs during the restored period, the "downward pressure on the price of existing drugs" from the "increased supply of new medicines," and the "substantial savings over other forms of health care" that can be provided by new drugs. (pp. 7 & 44)

VIEWS OF GOVERNMENT AGENCIES

The Patent Term Restoration Act has been supported by the Patent and Trademark Office, the General Accounting Office, and the Food and Drug Administration, on the grounds both of equity and of the need to stimulate the development of new drugs.

Patent and Trademark Office

The Commissioner of Patents and Trademarks has testified in support of the legislation:

"Our support of the bill is based on the premise that the patent system will provide a healthy stimulant for investment in research and development only if its incentives are not unfairly curtailed. Given the progressive increase in the loss of commercial exclusivity caused by Federally mandated testing and regulatory review requirements, we can no longer ignore the fact that certain sectors of our industry are denied the full benefits which the patent system was intended to provide.

Inventions in agricultural chemical technology, and even more so in the pharmaceutical field, depend heavily on patent protection. Development of such inventions is extremely costly, yet their imitation is often simple and inexpensive. * * * However, to the extent that a shortened effective patent term lessens the incentives of industry to continue making large commitments toward research and development, we should move to ensure that these incentives are restored. Effective patent protection is a necessary prerequisite to pharmaceutical and chemical research, given the enormous costs and risks involved. Enactment of this bill would go a long way toward making that protection effective again.

If we are to reverse our declining rate of innovation, we cannot afford to make our patent system progressively less attractive to important sectors of research intensive industry. * * * Enactment of the Patent Term Restoration Act would redress an inequity by restoring to patentees a part of their patent term which has been eroded by Federal premarket regulatory review. Given the proposition that the patent term is a form of compensation to the inventor for having fully disclosed his invention to the public, one inventor should not be treated differently from another. The Federal government should not induce full public disclosure of an invention through a patent grant of seventeen years, and then reduce the effective life of the patent through premarket regulatory review procedures.

Opponents of this proposed legislation have argued that the problem which the bill would alleviate has not been demonstrated.

They have pointed to high profit margins of industries which would benefit from this bill and have concluded that, as a consequence, there is no problem. I would suggest that the patent system not be misused as an economic regulator of U.S. industry. To establish different effective patent terms depending on the potential economic success of a particular sector of technology is not an approach I would recommend. And to fail to stem the erosion of effective patent terms due to Government regulations is just as unfair. Accordingly, there is a demonstrated problem: certain sectors of our industry, dealing with technologies which are subject to premarket regulatory review, are not receiving the full benefit of the patent system to which they are entitled by virture of having disclosed their inventions to the public.

Concern has also been expressed that the proposed legislation would further increase the noncompetitive period of exclusivity. Such concerns assume that the period of patent exclusivity is necessarily noncompetitive. But in general, patented products in the market are not completely free from competition. They often compete with other similar patented or unpatented products in the same field of application and are not instant financial successes solely on the basis of having been patented. They are, however, protected from slavish imitations and that protection should be continued for an effectively full patent term.

Opponents of the Patent Term Restoration Act speculate that its enactment would not guarantee the expenditure of greater resources into research and development. Proponents of the bill, on the other hand, note that significant shortening of the patent term, while not the sole reason, has had an adverse effect on research and development investments. I cannot categorically state that patent term extension will significantly increase innovation. I do stress, however, that throughout the many years of its existence, our patent system has encouraged innovation through the incentives it provides. It is a logical deduction that as these incentives are diminished, so is the encouragement which the patent system might otherwise have provided.

Proponents and opponents of this bill have significantly different opinions regarding the actual effective patent life presently accorded to pharmaceuticals. Studies have been cited to show that the effective life of a pharmaceutical patent is about 9.5 years. Others refute this claim by stating that the real average lies somewhere around 18.5 years. Those who assert that the average life of a pharmaceutical patent is greater than 9.5 years, do so on the basis that the effective patent life has been calculated by measuring only the date of the earliest patent issued. They maintain that by obtaining later patents on the same technology, the patentee increases the effective patent life of the product, thereby maintaining an unwarranted market advantage. This practice has been labeled 'pyramiding' or 'the evergreening of patents'.

It is claimed that patentees can prolong their protection by obtaining process and use patents after having been granted a patent on the product itself. While it is certainly possible to obtain additional patents, one should be clear exactly on what basis those patents are obtained and what kind of protection they afford. First, any patent issued must be patentably distinct from any other patent, which is to say, it must contain a different invention. If someone first obtains a product patent and later discovers another unexpected and patentable process for the use of this product, he is entitled to protection of his invention. This is not an extension of the original patent or a merely obvious variation of the original invention; it is a separate and distinct invention, capable of being patented in its own right.

The same applies to a new discovery of a process for the manufacture of the originally patented product. If such a process is a separately patentable invention it is entitled to protection. In such a case, the patentee of the original product has not extended the patent term of his product, he has made new inventive contributions to the technology.

He is therefore entitled to protection in turn for having publicly disclosed his invention.

However, what does a patent on a new use for a product or on a new process of making a product convey to the patentee? Regulatory review aside, if the original patent on the product has expired, the public is free to manufacture that product for all the uses for which the product was originally intended, as well as for any other use, except for the newly patented one. If a patent for a process of manufacture was also obtained, this particular new manufacture is protected, although the public is free to make the product in any other manner. As a consequence, the product itself does not enjoy continued and evergreening patent protection.

Lastly, it must be recognized that practical enforcement of use patents, and of process patents, is difficult. In the case of a protected use, unauthorized substitution is very hard to police. Patents which cover processes for manufacture are equally difficult to enforce. As a consequence, I find the allegations of patent pyramids difficult to accept, and would tend to favor the view that full protection of a particular product on the market depends upon the product patent itself and upon its effective patent term.

While I would welcome the streamlining of premarket regulatory review procedures, I do not think that they can be compressed sufficiently to provide adequate relief for patentees whose effective patent terms are eroded, and at the same time be fully satisfactory to safeguard health, safety and the protection of the environment. There is no reason, however, why both objectives cannot be met. Adequate regulatory review is a matter of necessity. At the same time, it is equally important that pharmaceutical and agricultural chemical industries be afforded the same protection and benefits of

> the patent system as are available to innovators in other technologies."[53]

General Accounting Office

A letter dated June 5, 1981 from the Director of the GAO to Senator Mathias provided support for the legislation:

> "Economic analyses of the determinants of Research and Development (R&D) expenditures in the pharmaceutical industry indicate that these outlays are quite sensitive to both expected returns and the availability of internally generated cash flow. The proposed increases in patent term would have positive impacts on both these determinant variables. The average effective patent term for new product introductions is now approximately 10 years in length and declining over time. One sensitivity analysis, based on a sample of all new product introductions in the U.S. over the period 1970-76, indicates that from 12 to 19 years of product life was necessary for this group of new drugs to break even and earn a competitive return on capital. The effect of increased patent terms on the expected returns to drug innovation was also highly sensitive to the degree of substitution faced by the pioneering firm's product after patent expiration. The degree of substitution has been increasing over time as a result of the enactment of State product selection laws (allowing pharmacists to substitute for prescribed brands) and the Federal Government Maximum Allowable Cost (MAC) program on medicaid and medicare reimbursements.
>
> The current environment for drug innovation therefore combines higher R&D costs and longer development times with increased potential competition from generic products after patents expire. Given these trends and the findings of various economic studies on R&D returns, it

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[53] Statement of Gerald J. Mossinghoff, Commissioner of Patents and Trademarks, before the Subcommittee on Courts, Civil Liberties and the Administration of Justice, Committee on the Judiciary, House of Representatives 3-8 (November 12, 1981).

> is reasonable to expect that the term of patent protection will become an increasingly important economic incentive influencing R&D decisions in future periods. It is more difficult to say, however, what type of pharmaceutical R&D would be most stimulated by increased patent terms and what kind of new drugs would be made available (or made available sooner) from patent restoration. From a theoretical standpoint, patent restoration can be expected to have its greatest impact on R&D incentives for products with relatively long expected lives before they are made obsolete by rival innovations. If a drug has a relatively short expected life before technological obsolescense occurs, it would be essentially unaffected by patent restoration. Hence, one class of drugs that would be positively affected by patent restoration are 'break-through' type drugs which have above average riskiness but longer expected product life before obsolescence. Quantitative effects in this regard are uncertain however." [54]

The Chief Medical Advisor of the GAO has discussed these views further:

> "The 17 year patent term has remained unchanged in this country since 1861. It represents, of course, a judgement as to a desirable length of time to permit the public to benefit from the innovations that can be stimulated by granting exclusive rights to the inventor. No one can prove that 17 years should be considered the perfect time period. However, it is clear that, in the case of drug innovation, the period of exclusive marketability is currently much less than 17 years and indeed is often closer to 7 years. This is partly because final FDA approval may take several years. This matter takes on added significance when one considers that it now costs an average of $70 million for each new drug entering the market

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[54] S. Rep. No. 97-138, 97th Cong., 1st Sess. 10, 11 (1981) (footnote omitted).

place. Thus, the incentives to invest in pharmacological research and development are somewhat less than would be true if 17 years of exclusive marketing were to apply. This lengthy time taken for drug approval is a fairly recent occurrence. Twenty years ago, the process took about 2 years as compared to between 7 and 10 years today. Clearly the emphasis on ensuring safety and efficacy, important as it may be, has taken its toll.

GAO's position on this issue was summed up in a letter addressed to the Chairman, Senate Judiciary Committee earlier this year. In that transmittal, we expressed the view that increases in patent term should have a positive impact on both monetary return and internally generated cash flow for the pharmaceutical industry. We suggested that this, in turn, would undoubtedly stimulate research and development and eventually result in an increase in new drug innovation.

We further reasoned that we would expect that the patent protection term would become an increasingly important economic incentive influencing research and development decisions in the future. 'Breakthrough' type drugs would have a particular propensity for being positively affected by patent restoration since they tend to have above average risk but longer expected product life through obsolescence.

It was also our opinion that patent restoration would have a significant affect on new drug prices because of the fact that those drugs would be able to maintain an exclusive market for longer periods of time. Hence, the savings that consumers obtain through price competition would likely be deferred. Accordingly, it was our judgement that, on balance, consumers would benefit financially to the extent that the gains on innovation stimulated by patent restoration exceeded the increased costs from higher drug prices. This, of course, is in addition to the possible gains in relief of human suffering which result from increased drug innovation."[55]

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[55] Grant, Progress and Problems in FDA's Drug Approval Process 10-12 (December 15, 1981).

Department of Health and Human Services
And
Food and Drug Administration

In a letter dated August 18, 1981 to Congressman Rodino, Chairman of the House Committee on the Judiciary, Secretary of Health and Human Services Schweiker endorsed the legislation:

> "In summary, we support the bill. We believe that it corrects an inequity in the patent laws of the United States and is among the initiatives that will help to encourage innovative research and the development and marketing of important inventions pertaining to public health and safety.
>
> * * *
>
> * * * The patent incentive is particularly important in the case of new drugs which have a relatively limited market potential but which require extensive and expensive development and testing before the invention can be marketed, to document utility, safety, and efficacy in order to comply with the requirements of Federal statutes and regulations."

The Commissioner of Food and Drugs has testified in support of the bill:

> "The Department already has expressed support for patent life extension legislation, now pending in the Congress, as a means of preserving innovative pharmaceutical research. New drugs generally require extensive and expensive development and testing before they can be marketed. In an industry where high development costs and risk of failure are standard and small potential markets are not uncommon, it is important to preserve incentives for investment and innovation.
>
> We are working to reduce the premarket approval process time by revising the new drug regulations . . . Regardless of the outcome of these efforts, our premarket approval system must continue to be thorough enough to assure the safety and efficacy of new drugs, even if that means living with a process that takes

longer than we would ideally prefer. We cannot encourage innovation, at the expense of safety.

* * *

I would also emphasize that the last few decades has seen an extensive evolution in science and medicine and this has increased enormously the complexity of drug development. New drug development in the future is going to be an even more technically complex and expensive process. When considering the adequacy of incentives for innovation, we need to recognize this long-term trend.

Another need to be recognized is that involving a group of drugs that has perhaps suffered more than any other in the drug development process. Known as 'Orphan Drugs' or drugs having low commercial interest, their unavailability has been a public issue for several years. FDA has chaired the Interagency Task Force on Significant Drugs of Limited Commercial Value, which in its report of June 29, 1979 presented a number of options for dealing with the problem. We are now cooperating with the Commission on Drugs for Rare Diseases sponsored by the Pharmaceutical Manufacturers Association. While progress is being made, any steps taken to encourage innovation would hopefully be of value in alleviating this problem.

In summary, Mr. Chairman, an extensive amount of information is required to support the approval of a new drug for marketing. But requiring such information does take time and money. The average time from the synthesis of a new molecular entity to its approval for marketing as a drug is on the order of 8 to 10 years. The average time for development of innovative dosage forms and minor chemical variants (e.g., salts or esters) of already established entities is probably somewhat less.

These long, development times have led to safer and better products, but they also may adversely affect innovation by cutting into the patent lives of drugs. For this reason, the Department has supported the principle of patent life extension as a matter of equity

> to drug manufacturers and as an incentive for innovation."[56]

In a recent interview, the Commissioner expanded upon these views:

> "'I have taken the position, and it is consonant with Secretary Schweiker's, that innovative research by creative development firms is important. They are the suppliers of new drugs to this country. And in other countries where other systems have been tried, they have not worked. So drug companies must have a reasonable return on their money investment because the state of science and [meeting] the expectations in drug development are terribly expensive. Otherwise, as with any other company, they will dry up and blow away.
>
> 'There is no question time is lost because of our drug development and approval process. But, whether it takes five years or 10 years, and it varies from drug to drug, nobody expects to get rid of premarketing approval. Patients, physicians, everybody expects that when a drug goes on the market it is safe and effective. * * *
>
> 'The question is,' says Hayes, 'how are the drug companies going to get a return on that investment if there is, by public demand and scientific ability, time lost in the necessary development? That time will never be zero. It seems to me patent restoration is obvious.'"[57]

CONCLUSION

PMA believes that, with a restored patent term for pharmaceutical products, the real cost of safe and effective and effective therapy will not increase, and is likely to decrease. But for consumers, the most important question is whether, absent patent restoration, the new therapy will exist at all.

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[56] Statement by Arthur Hull Hayes, Jr., M.D., Commissioner, Food and Drug Administration, before the Subcommittee on Courts, Civil Liberties and the Administration of Justice, Committee on the Judiciary, House of Representatives 1-2, [illegible]-7 (November 5, 1981).

[57] "FDA's Hayes: Goal Approach to Regulation," Chemical and Engineering News, January 18, 1982, pp. 45, 48.

From the public viewpoint, the critical factor is not patent lives or research investment -- it is safe and effective new medicine. The erosion in NCE drugs parallels the erosion in patent life and research investment. In 1960, a $3.5 billion industry with effective patent lives averaging 16 years produced 50 new medicines. In 1980, a $22 billion industry with effective patent lives averaging less than eight years produced only 12 new medicines.

This unfortunate situation is not the product of congressional design. Nor has FDA set out to reduce the effective patent lives and the industry investment in pharmaceutical innovation. No one could have anticipated that a testing and approval process which took about two years in the early 1960's would take seven to 13 years in 1980. Reduced patent protection for drugs has evolved by accident, and until recently with little notice.

Innovation and price competition are not mutually exclusive. They are complementary. The experience with our patent system for over a century has demonstrated that a 17-year patent life provides for innovation and competition for all products in all industries. For pharmaceutical products, the effective patent life has been eroded to less than half what it once was and what Congress intended it to be. The balance between innovation and price competition struck by Congress has therefore been upset, and the public health is suffering as a result.

We believe it is in the public interest to restore this balance. PMA therefore strongly supports the Patent Term Restoration Act, which would again provide the incentive needed to invest in pharmaceutical innovation in this country.

The concept of patent term restoration has been studied at length and in depth. All of the factual information and policy analysis needed by Congress to resolve the matter has been made available and extensively reviewed. There has been a report by the Office of Technology Assessment and numerous congressional hearings. It is time for Congress to bring the matter to a decision.

Those who oppose patent term restoration legislation have, of course, continually asked for further information and further study. They want it studied to death. They want, at all costs, to avoid a resolution of the matter. This is only a diversionary tactic. During a recent public interview, Secretary Schweiker was asked about doing a further study on patent term restoration. He responded:

> "I'm not sure that that isn't a subterfuge that some people are using just to slow the whole process down. It seems to me it's a pretty simple straight forward question. That either

> you have lost some time because of the drug approval process or you haven't. I happen to believe we have."[58]

PMA agrees. All of the pertinent facts and arguments have been identified, and the matter should be decided by Congress now.

Mr. Chairman, this concludes my prepared statement. I would be happy to answer the Subcommittee's questions.

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[58] "Interview with HHS Secretary Schweiker," FDC Reports, January 18, 1982, pp. 21-22.

PHARMACEUTICAL MANUFACTURERS Association

1155 FIFTEENTH STREET, N.W.
WASHINGTON, D.C. 20005
AREA CODE 202/463-2000
CABLE: PHARM/WASHINGTON, D.C.
TELEX 248498 PHAR UR

February 4, 1982

NEW OTA PRESENTATION SUPPORTS PATENT TERM RESTORATION ACT

The information to be presented today by the Office of Technology Assessment (OTA) confirms the need for the Patent Term Restoration Act (H.R. 1937).

First, the OTA data show an average "regulatory period" (calculated by OTA from FDA receipt of the IND to FDA approval of the NDA) of 8.3 years. This is longer than prior estimates by FDA and others.

Second, the data show that, under the Patent Term Restoration Act, the patents for these drugs would have been restored an average of 5.7 years. This is 2.6 years less than the average regulatory period calculated by OTA for these drugs.

Third, the OTA presentation confirms that, for these drugs, the average effective patent life (EPL) is 7.4 years. Under the Patent Term Restoration Act, the average effective patent life, after restoration, would have been 13.1 years for these drugs. This contrasts with the statutory 17 years for patents.

Fourth, OTA found no correlation between the regulatory period and the EPL for these 12 drugs. OTA did find a correlation between the EPL and the period from patent filing to IND receipt. This correlation, however, is irrelevant under the Patent Term Restoration Act. Any delay before a drug enters the regulatory period hurts the patent holder because it results in no patent term restoration.

A tabular summary of the OTA data on the 12 new chemical entity (NCE) drugs approved by FDA during 1980 is attached.

1980 FDA Approvals of NCE Drugs

Drug	Patent Filed	Patent Issued	Preclinical Period		OTA Regulatory Period			Effective Patent Life (days)	Patent 4/ Restoration Under H.R. 1937 (days)
			Patent Filed 1/ (days)	Patent Issued 2/ (days)	IND Received	NDA Approved	IND/NDA Time 3/ (days)		
Viroptic	9/18/63	8/17/65	3955	3256	7/17/74	4/10/80	2094	855	2091
Meclan	12/19/60	5/16/61	5729	5581	8/26/76	5/30/80	1373	0	0
Cinobac	2/4/69	6/13/72	1280	55	8/7/72	6/13/80	2867	3283	2555
Mec:omen	1/21/61	4/11/67	1470	-810	1/21/65	6/25/80	5634	1381	2555
Vansil	5/29/68	6/28/74	835	-1386	9/11/70	7/23/80	3603	3988	2226
Calderol	3/17/69	9/3/74	1560	-436	6/24/73	8/5/80	2599	4042	2185
Yutopar	2/25/65	11/12/68	2247	891	4/22/71	8/29/80	3417	1897	2555
Asendin	2/28/64	8/1/72	2121	-956	12/19/69	9/22/80	3930	3231	2555
Zomax	7/26/67	8/14/73	2553	342	7/22/74	10/28/80	2290	3573	2288
Siseptin	6/27/68	9/23/75	1670	-974	1/22/73	10/29/80	2837	4342	1765
Ludiomil	11/9/61	8/27/68	2713	230	4/14/69	12/1/80	4249	1726	2555
Spectrobid	9/7/71	3/26/75	1895	600	11/14/76	12/22/80	1499	4106	1498
Average (in days)			2335.7	532.8			3032.7	2702	2069.0
Average (in years)			6.4	1.5			8.3	7.4	5.7

Total Effective Patent Life
Under H.R. 1937: 13.1 years.

1/ Preclinical Period = ~~NDA~~ IND Receipt Date - Patent Filing Date.
2/ Preclinical Period = IND Receipt Date - Patent Issue Date.
3/ IND/NDA Time = NDA Approval Date - IND Receipt Date.
4/ Maximum Patent Term Restoration = 7 years or 2555 days.

Mr. GORE. Thank you very much, Mr. Hutt.

On page 50 you just talked about the erosion of research investment. Further down on the page you say that you do not believe that FDA has set out to reduce industry investment in pharmaceutical innovation. On page 32 toward the bottom you say it is not surprising that investment and innovation have declined, and on page 5 you talk about a decrease in real R. & D. investment by the industry.

Mr. HUTT. Yes, sir.

Mr. GORE. Has there been a decrease in R. &. D. investment by the industry?

Mr. HUTT. If you will refer to figure II on page 4, I believe that you will see the documentation for that. The solid line represents R. & D. as a percent of sales, but it does not reflect inflation. If you factor in inflation, you find the dotted line constantly decreasing, showing R. & D. as a percentage of U.S. pharmaceutical sales to the point where it is now very low in relation to sales. The reason for that is that the cost of R. & D. has escalated much, much higher than drug prices. In our testimony we point out how remarkably stable drug prices have been at the same time that research costs have gone up at the normal rate of inflation.

Mr. GORE. Are you saying that while it may appear to a casual oberver that R. & D. expenditures by the industry have been increasing, actually when you correct for inflation the amount of money spent by the industry on R. & D. has been going down?

Mr. HUTT. Yes, across the entire industry. Individual companies may——

Mr. GORE. Let me stop you right there. You are saying across the entire industry the amount of R. & D. money being spent when you adjust it for inflation has been going down?

Mr. HUTT. As a percent of sales.

Mr. GORE. What if you asked the question—see, this is a little tricky. You do not say as a percentage of sales.

Mr. HUTT. I am sorry. The heading on figure II——

Mr. GORE. Let me refer you to page 32. You say it is surprising that investment and innovation have declined. On page 5 you say, "Coupled with a decrease in real R. & D. investment by the industry, it is not surprising * * *" and so forth. And on page 50 you refer to reduction in industry investment in pharmaceutical innovation.

Mr. HUTT. I thought that was modified by the original statement on pages 2 and 4. We made it clear we were talking a percentage of U.S. pharmaceutical sales.

Mr. GORE. Well, that is a little tricky, is it not?

Mr. HUTT. I do not think so, because people have been saying and you read the OTA report to say that as a percent of U.S. pharmaceutical R. & D. expenditures we were having constant investment, and that simply is not true.

Mr. GORE. No. The fact is, contrary to what a casual reader of the statements on page 50, page 32, and page 5 might receive, the fact of the matter is there has been an increase in real R. & D. spending by the industry. Is that not the fact?

Mr. HUTT. I do not have the figures.

Mr. GORE. Let me cite the OTA report. Have you got it there?

Mr. HUTT. Yes; I do.

Mr. GORE. Page 34.

Mr. HUTT. Yes; I have page 34.

Mr. GORE. Table 12. You served as one of the reviewers of this report, did you not?

Mr. HUTT. Yes.

Mr. GORE. It shows that——

Mr. HUTT. That is the total domestic and foreign R. & D. I do not have the domestic R. & D. pharmaceutical figures, Mr. Gore.

Mr. GORE. All right. I will supply this for the record. The domestic spending shows the exact same trend. When you separate out domestic and foreign there is an increase in the amount of money spent on research and development. When you adjust for inflation and use the same deflator that you suggest be used in your table, there is still an increase, and a substantial increase, in the amount of real investment in research and development by the drug industry.

Mr. HUTT. I simply do not have those figures, Mr. Gore. I cannot comment on that.

Mr. GORE. Well, this—these statements should not be——

Mr. HUTT. Let me emphasize, that shows domestic and foreign. I do not—as I said, I do not have the domestic figures.

Mr. GORE. Let me refer you to table 5 on page 28.

Mr. HUTT. That is right, they are there.

Mr. GORE. Now, you reviewed those figures, did you not?

Mr. HUTT. I read them at the time, yes. I did not review them for accuracy.

Mr. GORE. You did not provide any comments to change them?

Mr. HUTT. I would have no basis for doing it.

Mr. GORE. You were given an opportunity to provide comments on the report and did provide comments on many sections of the report?

Mr. HUTT. Yes; I did, but I have no basis for agreeing or disagreeing with figures like this.

Mr. GORE. They seem to be important figures if they indicate that contrary to the impression that has been given the Congress by the pharmaceutical industry in fact the real investment in R. & D. has been steadily increasing. It seems to me you might be interested in that figure. You do not challenge it, do you?

Mr. HUTT. Certainly not. I have no reason to disbelieve them. I simply was clarifying that I did not personally have information to believe or disbelieve the figure, Mr. Chairman, but I have no reason to quarrel with that figure. I can state, and I would repeat—and this was all that we did say in our statement that R. & D. decreasing as a percent of sales. What OTA failed to point out when they said that it was steady as a percent of sales was that in real terms that meant a reduction, because they failed to take the deflator into account there.

Mr. GORE. Perhaps the statement on page 5 should read coupled with an increase in real R. & D. investment by the industry instead of coupled with a decrease. Would you accept that amendment to your statement?

Mr. HUTT. I would say coupled with a decrease as a percent of sales, and that nonetheless results in a net increase in R. & D. investment, yes.

Mr. GORE. On page 32——

Mr. HUTT. But what it is important to understand and what many people do not realize is that when the percent of sales devoted to R. & D. remain steady, that does not mean that you get the same number of NCE drugs. You get fewer and fewer every year unless you compensate for that.

Mr. GORE. Well, I think it is quite significant, extremely significant, that contrary to the impression given to the Congress in statements like this for some time now, actually the truth of the matter is that real spending for research and development has continually increased. Now——

Mr. HUTT. Mr. Gore, I think one aspect that one must not forget are the figures that were given by Dr. Wardell that the kind of investment that one is making in the U.S. pharmaceutical industry today is changing. Fewer and fewer drugs are being synthesized and originated in the United States. More and more are coming from abroad, and this reflects the decrease in certain respects of innovation in the United States.

Mr. GORE. Well, now, let us turn to that. OK. I made the point that I wanted to make here and I will not belabor it on page 32 and page 50 and page 2, there ought to be appropriate changes throughout your statement to indicate that in fact R. & D. spending has not decreased, it has increased. With respect to innovation I want to accept your definition of innovation which you cite at the beginning of your statement, "Economists define technological innovation as the initial commercial application of a new product or process." Then you go on to say that innovation since 1962 has declined, and you provide figure 1 on page 3 to support that statement?

Mr. HUTT. In 1962, that was the year of the greatest decline.

Mr. GORE. Well, but since 1962——

Mr. HUTT. I should have said since 1956 or 1959 or 1960.

Mr. GORE. Well, we will change that. Should we change that in the statement, too?

Mr. HUTT. I would still stick with 1962 because the decline came in the 1962 era.

Mr. GORE. It is hard to fuzz that over.

Mr. HUTT. We have not reached the same level as the level of 1962.

Mr. GORE. Oh, really? What was the number in 1962?

Mr. HUTT. I believe it was 30.

Mr. GORE. In 19—the line—let us take 1963 then. In 1963 it looks like it was about 18.

Mr. HUTT. That is correct.

Mr. GORE. How many was it last year?

Mr. HUTT. Last year it was 27.

Mr. GORE. That is not a decrease.

Mr. HUTT. Yes, but 1963 was 18. 1962 was 30. If you note, they go up and down since 1963.

Mr. GORE. Since 1962 there has been no decline, has there?

Mr. HUTT. Well, 1962 was 30 and 1963 was 18.

Mr. GORE. Since 1962.

Mr. HUTT. Yes; there has been.

Mr. GORE. Since the new law there has been no decline.

Mr. HUTT. Since 1963 there has not been, but since 1962 there has been.

Mr. GORE. After the new law, after 1962, there has been no decline——

Mr. HUTT. Excluding 1962?

Mr. GORE. Since the new law took effect.

Mr. HUTT. If you begin with 1963 there has been a steady rate of NCE approvals.

Mr. GORE. In fact, last year there were more approved than in any year since 1962?

Mr. HUTT. By a slight margin. As Dr. Hayes said, that shows no trend at all. We are delighted that there were more in the pipeline for approval. We hope next year there will be not only 27, but perhaps 57. Dr. Hayes and Dr. Crout are the first to point out that that is unlikely to occur.

Mr. GORE. The fact of the matter is that R. & D. expenditures have increased and innovation has not declined, so——

Mr. HUTT. But it has not increased, either.

Mr. GORE. It did last year. As you define it in your statement. So I really do not see where your case is.

Mr. HUTT. If you take from 1963 to the present and average it out you will see as you stated roughly a straight-line trend. There has been no increase and no decrease. Admittedly in a process like this it will go up and down. Our point is that we are not going to see an increase that will even remotely reflect an increase in investment for some years to come.

Mr. GORE. OK.

Mr. HUTT. Unless we have some incentive to increase that innovation.

Mr. GORE. OK. Well, should we or should be not change your statement on page 2, "During the period from 1962 to the present, pharmaceutical innovation in the United States has declined substantially?" Should we modify that?

Mr. HUTT. I think not, because beginning in 1962 we had 30 drugs approved, and we have not had that much since.

Mr. VOLKMER. Would the Chairman yield?

Mr. GORE. Be glad to.

Mr. VOLKMER. I have to leave. I have another appointment at 4:30, and I wanted to ask a question of Mr. Hutt on something that I think he has confirmed as to my discussions earlier this morning with OTA, and now that I have had time to finish up on the time period which OTA said was very significant, which was the time from the patent filing to the time of the IND submission was received, I have averaged that out over those same 12 drugs that they had on these charts up there and that they have submitted, and I find that that is only 4.4 years on all 12 of those, I find that the time period of possible delay, that is allowing for 2 years for testing on each one from the time the patent is filed.

Mr. HUTT. Yes, sir. My figures show exactly the same.

Mr. **Volkmer**. And then on the time period, the average time period for regulatory delay as we call it, for FDA approval from IND to NDA approval, I find it averages out to 8.3 years.

Mr. **Hutt**. That is true.

Mr. **Volkmer**. What I cannot understand from OTA people, and I hope they can explain it in their letter, is why 4.4 years is more significant a delay than 8.3 years. Can you perhaps help me on that? How can 4.4 be a more significant time period than 8.3, when both of them you cannot market the drug?

Mr. **Hutt**. Mr. Volkmer, I am in complete agreement with you. I do think it is a matter of simple arithmetic.

Mr. **Volkmer**. Unless somebody is biased and not being objective in their analysis.

Mr. **Hutt**. I also pointed out a few moments ago that the assumption that 2 years is sufficient for all preclinical work is an unwarranted assumption.

Mr. **Volkmer**. Even assuming that, we still come to that conclusion.

Mr. **Hutt**. I agree with you, sir.

Mr. **Volkmer**. Thank you, Mr. Chairman.

Mr. **Walker**. Would you yield?

Mr. **Gore**. Sure.

Mr. **Walker**. I, too, was bothered by the chart that was on page 3. When you start comparing the 1982 to 1981 timeframe, it seems to me that there is a problem there with regard to proving the case. However, it seems to me also that the problem in this regard has become most acute since 1975, that while it is true if you want to use the years and so on depending upon how you juggle the years here it makes a difference. But we are looking at the fact that the regulatory process has tended to become tighter and tighter down through the years, and I think that is reflected in the chart that you have on page 18. If I understood your testimony correctly, and then looked at the chart on page 18. We found that the trends in IND duration were going up, particularly in the time frame of 1975. They take a dramatic increase there, and you attributed that to the fact that the requirements were becoming more rigorous and more demanding during that period of time, FDA. Is that a correct interpretation of that?

Mr. **Hutt**. I believe that it is almost a straight line from 1966 to 1976. That small aberration would show those little dips and peaks. It is hard to pick any 1 year.

Mr. **Walker**. If indeed there was more rigorous—if those IND duration times were becoming more rigorous because of more rigorous regulations, if you look at the chart on page 3 it becomes apparent that we have had a severe problem since 1975, because there has been a downward trend since 1975, when the IND time took a jump. Then it drops off to 1980, and then there is an aberration in 1981 as Dr. Hayes testified, but the general trend has been downward.

It seems to me that that is what led to the present legislation that is before us. The legislation that is before the House is a result of that declining trend over the last 5 or 6 years, and that is what we are being responsive to, so it depends on where you want to start on these charts, whether you want to start in 1962—the chairman picked 1962 as one factor. The fact is in 1962 we are just getting started with the process, but the regulations have become tighter and tighter. I think in 1975 shows for the last 5 or 6 years we have had a steady downward trend until the present aberration. I think the chart should reflect that the present situation is a situation caused by a problem that has developed over the last 5 years or so.

Mr. HUTT. I would comment only that I would not like to get hung up on the question of which year was the best or the worst or which year for example, Mr. Gore, do you actually have the break point from the good old days to the present problem of a reduced approval of NCE's. I am perfectly willing to accept your criticism that we could have moved back a year on the date of 1962, and I apologize if you feel that we overstated that. The point is if you look at figure 1 on page 3, and you take any kind of an average from 1950 to 1960 and compare it with any kind of an average from 1962 to the present, we are looking at the difference of day and night. And what we need is to find a way in this country to get back up from wherever we are at the moment, back up to where we were in the 1950s. And that we believe can be done through the Patent Restoration Act.

Mr. GORE. Well, you support the 1962 law; do you not?

Mr. HUTT. Yes; indeed I do.

Mr. GORE. You would not want to go back to a time when there was no efficacy?

Mr. HUTT. PMA has not suggested that efficacy ought to be deleted from the law or that there ought to be a diminution of requirements. We are working with your Commission, working with FDA to improve the present system, but we do not favor deleting the efficacy requirement.

Mr. GORE. A couple of other things that give me some problem with your statement. You talk about the unbelievable figure of $70 million in reference to the cost of bringing a new drug to the market, and you compare it with a $6 million figure in 1982. That certainly seems like a striking increase. Are those two figures comparable? Were they calculated in the same way, or is there something tricky about that?

Mr. HUTT. My understanding is that they were calculated in the same way. Perhaps I can help you understand how they are calculated. They do include the cost both of drugs that get to market and of drugs that do not get to market, because the drugs that do get to market and achieve a profit must have sufficient profit to compensate for the drugs that do not get to market. So these are the costs averaged over all of the drug research efforts.

Mr. GORE. Now, there are two different studies cited, one study for the $6 million figure, and then another for the $70 million figure. It is my understanding that the two calculations are completely different. For example, the study by Mr. Hansen cited for the $70 million figure includes $21 million labeled opportunity cost of capital that is nowhere reflected in the calculation of the first figure. And there are a number of other problems of comparability as well. If you are not familiar with that, I will hold the record open.

Mr. HUTT. We will be happy to supply information on that rather than taking time to look it up now.

Mr. GORE. It is just apples and oranges. You do not know any reason to challenge that statement here?

Mr. HUTT. I do not think that the figure of $6 million would be changed significantly if one did that kind of calculation, Mr. Gore.

Mr. GORE. Well, proportionately it certainly would.

[The information follows:]

Mr. Hutt subsequently advised the subcommittee that, in his view, adding a cost of capital to the Baily figure would increase that figure from $6 million to $7 million in 1962 dollars and from $16 million to $20 million in 1980 dollars.

Mr. GORE. On page 38 you quote OTA as saying, "Since 1966, average effective patent terms have declined * * *"—dot dot dot. I used to be a journalist, and I always am very careful with those dot dot dots, so I went and looked at what the dot dot dot was, and it says "however"—that is the next word. Excuse me, "have declined." Next is, "Some factors influencing effective patent terms are, however, changing and there is reason to believe that the decline may be halted in the future." Do you agree with that statement?

Mr. HUTT. I would say at some point they have to halt. They cannot go down lower than zero.

Mr. GORE. Do you agree there is reason to believe that the decline may be halted in the future?

Mr. HUTT. Mr. Gore, I would not have believed that they would get down to 6.8, which we heard as the 1981 figure from Dr. Wardell. I hope that trend will be halted, but at this moment I do not see what will halt it other than the Patent-Term Restoration Act. We can hold the line perhaps, particularly to the extent that FDA can improve slightly upon the regulatory review process, but I am afraid, as Dr. Hayes testified, both the time needed to prove the safety and effectiveness of a drug and the time to review that will forever remain very, very substantial.

Mr. GORE. Now, the preclinical stage and the assumption of 2 years as a reasonable figure or as a general figure in the OTA analysis that I asked be done—you criticized that in your initial statement. The source of that is the OTA-approved study, of which you served as a reviewer, that says on page 14, under "Drug Development, the Preclinical Stage," "The preclinical stage generally lasts from 1 to 2 years," and I am informed that that comes from the industry and from sources such as Dr. Wardell.

Mr. HUTT. Let me say that I have asked my colleagues in PMA if they ever said this or were ever asked about this, and they are not aware that they ever said this or were asked about this. I would not have said 1 to 2 years. I can only state that when I reviewed this I may have passed over it without noticing it, or I may not actually have reviewed this particular statement. The House subcommittee report says 1 to 4 years, and I really think that that is fairly optimistic.

Mr. GORE. That was done prior to the changes being implemented by Dr. Hayes as well, the SRT report that you refer to, was it not?

Mr. Hutt. Yes, but the changes implemented by Dr. Hayes do not relate to the preclinical stage at all. They relate only to the NDA review stage.

Mr. Gore. Well, the Commission is addressing the preclinical.

Mr. Hutt. Yes, it is, and I hope they will be able to cut that down.

Mr. Gore. Now, going to the OTA analysis, there appears to be a rather striking correlation between the effective patent life and the period between patent application and the IND filing. If I could get somebody on the staff to put that back up there. I think it would be extremely useful to look at that relationship and the other relationships that quantify, but first of all, is that not a striking correlation?

Mr. Hutt. To be quite honest, I do not understand the correlation. Particularly, Mr. Gore, I do not understand its relevance.

Mr. Gore. It is a regression analysis that shows the correlation between the effective patent life and the time taken between patent application and the filing of an IND, and the similar—if staff could put up the next chart, a similar relationship does not appear between the regulatory period and the effective patent life. And in view of the results, I think it would be extremely useful and informative to examine this relationship for a long period of time, for the years since 1962 through 1980. And I am wondering if PMA would agree to supply the data from 1962 through 1980 so we could analyze that instead of just a single year.

Mr. Hutt. Let me address the first half of your statement, Mr. Gore, because our view, and we have thought about this a good deal since we got the data yesterday afternoon, is that this study has no relevance to the Patent-Term Restoration Act at all. All that the Patent-Term Restoration Act is aimed at is restoring part, and not all, of the regulatory review period.

Mr. Gore. Let me interject. If in fact the regulatory review period is not the significant factor leading to a decline, if in fact the period between patent filing and IND filing is far more significant, then the assumption on which the legislative remedy is based is called in question.

Mr. Hutt. I do not believe so. No, Mr. Gore, and again we must go back to the statute. We have seen through the data presented by OTA a time from IND filing to NDA approval of 8.3 years on an average. That is right off the top of the effective patent life. We do not need any more studies on that. We already know that. That is not going to change if we go back and look to 1962 or back to 1950 or any other time. The issue is, should there be——

Mr. Gore. Wait a minute. We do need more studies. I beg to differ, in my opinion, because all of the studies that you have cited operate from means. You take a mean and call that the significant trend, and it is really not, because as in the example I cited early in today's hearing, a mean obscures the real pattern which prevails in the industry by giving far too much weight to exceptional circumstances that bias the outcome of a mean analysis.

Mr. Hutt. Then let us take a range, which is what the OTA witness suggested this morning. If you take a range, the OTA witness said that the effective patent life for the largest selling drugs today, which were approved many years ago, was 11 to 17 years.

Let us take a look at what the effective patent life is of the drugs approved in 1980, 0 to 12 years. So we have two ranges, one 0 to 12, and the other 11 to 17. You do not need a statistical analysis——

Mr. GORE. Of course, you do. If you have a range of 0 to 12 and there is only one zero and the reason it is a zero is because the company decided it would be a zero, and then the rest of them have no relationship to the zero, of course you need more analysis. If you put your head in the stove and your feet in the refrigerator, on average you are very comfortable.

Mr. HUTT. Mr. Gore, where you have two ranges, and they literally overlap like that, no matter how many outlyers you lop off, you have got a clear difference. In our testimony we have plotted on page 27 all of the studies that are available in figure 4. We go back to 1966, where every study that has ever been done shows 14 years of effective patent life, and we come down——

Mr. GORE. All of those are means, every single one of them, correct?

Mr. HUTT. Yes, and things will vary around the mean.

Mr. GORE. Do you not think that it would be helpful to the Congress as it considers legislation that might have a multibillion dollar impact on the people of this country that we have a thorough analysis other than just a rough averaging, a mean that obscures the real pattern? Could you provide us the data so that we might conduct a regression analysis on the rest of the years involved?

Mr. HUTT. Mr. Gore, just as the two charts or three charts here have confused matters, I think that a regression analysis going back to 1962 would doubly confuse people.

Mr. GORE. Is your answer "No?"

Mr. HUTT. The answer is "No."

Mr. GORE. I must say that I believe that the industry, if it asks the Congress to approve a multibillion dollar change in a law that has existed for 120 years, is in a poor position to refuse to provide studies other than industry-financed studies. Let me change that—other than studies that reflect the industry's point of view and refuse to provide a committee of the Congress with information on the facts of the matter. Now——

Mr. HUTT. Mr. Gore, we have provided massive amounts of information. The industry provided to Dr. Wardell every bit of its information years ago.

Mr. GORE. Oh.

Mr. HUTT. You are asking us to go back and reinvent the wheel, do the same thing all over again, and for no discernible purpose. The information to be obtained has no bearing on the legislation.

Mr. GORE. I think it does.

Mr. HUTT. We do not.

Mr. GORE. The analysis indicates that the regulatory period has an insignificant correlation to the decline in effective patent life. What I am asking you to do is to provide additional information for years other than the single year of 1980 so that we can determine whether that pattern holds true for all of the years since 1962. Now, how can you refuse and then say oh, you will only be confused. We want to take this rough average, this mean analysis and ram it through the Congress without any further analysis that might just confuse you.

Mr. HUTT. Let us go back to the first principle. The first principle is that we are not asking for a change in the law to undo 17 years. What we are asking for is a restoration of what inadvertently has been taken away from the pharmaceutical industry. That amounts, as we have testified, to pure discrimination against the drug industry and has in addition severely harmed the public health, in our opinion. We are going to reap the harm of not having patent restoration in the form of poor public health.

Mr. GORE. But because this has created—well, it has not created a decline in research and development expenditures. It has not created a decine in profits. It has not created a decline in innovation since the new law passed in 1962.

Mr. HUTT. Dr. Crout testified in April that in his professional judgment there had been a decline in important new drugs in this country.

Mr. GORE. The OTA and the Commissioner of FDA have both testified otherwise. Here you have got a steady increase in expenditures, real expenditures for research and development, a steady increase in the profits of the industry. No decline in innovation. And an analysis by the OTA staff that shows there is an insignificant correlation between the regulatory period and the effective patent life, and you come here and say we want you to pass this thing real quick and we do not want to provide any more information, because it might confuse you. It sure might confuse us, because the facts are not as the Congress has been led to believe.

Mr. HUTT. I do not agree with you, Mr. Gore. I am concerned about providing irrelevant information.

Mr. GORE. Well, let us worry about that. We are capable of avoiding confusion at times. Let us try to weed out the irrelevant data. Let us be the judge of what is relevant and what is irrelevant. On what grounds do you refuse to give the information? Is it because you think it might confuse us?

Mr. HUTT. The information is not pertinent to this particular proposed legislation. Again, the purpose of the legislation is only to restore the lost regulatory time. It is not to restore lost preclinical time.

To the extent that, for example, the makers of Meclan unfortunately did not realize the benefit of that drug until many years went by, they lost their time. Under the Patent Restoration Act they would receive zero years of patent restoration.

Mr. GORE. Wait a second, Mr. Hutt. You said that the information I have asked for is not relevant to the patent term extension issue?

Mr. HUTT. Yes, sir.

Mr. GORE. What I am asking for is the date on which patents were filed on drugs since 1962. I am asking for the date on which patents were approved. I am asking for the date on which the regulatory process began so we can look at the allegation that the—how come you say that those three facts are irrelevant to the patent term extension legislation?

Mr. HUTT. Because the critical fact is the amount of regulatory time lost. The IND to an NDA. You know, you already have all the data that could conceivably be submitted.

Mr. GORE. No; we don't.

Mr. HUTT. On the loss of effective patent life.

Mr. GORE. Let me complete this. The date of the patent filing, the date of the patent approval, and the date the regulatory process begins and ends are directly relevant to the ability of the Congress to understanding whether or not this problem is as the industry alleges it to be, and you are refusing to provide that information.

Mr. HUTT. Mr. Gore, it is not directly relevant. That is where you and I disagree.

Mr. GORE. The time between patent and the regulatory period is not relevant to a piece of legislation that is designed to remedy a defective relationship between those 2 days?

Mr. HUTT. What is directly relevant to that is the amount of the effective patent life loss and the direct correlation with the FDA regulatory requirements which has been testified to by everyone who has ever appeared before any committee of Congress on this matter.

All we are asking for is partial restoration of the loss of time created by regulatory requirements. The preclinical time is not included in that. We are not asking for restoration of time that we have spent looking at a chemical to decide whether to commercialize it or not.

That is not in the bill, and gathering more information on that is not going to help one Member of Congress decide the merits of that bill. It will stall. It will provide for more time for people who want to kill the bill.

Mr. GORE. Not if you provide it expeditiously. We heard from—we heard that the analysis, that the regression analysis only takes a couple of days. If you could get it to us in a couple of days, within 4 days, we could have it done.

Mr. HUTT. Mr. Gore, if you will give us the data, we will be glad to do the regression analysis ourselves. It is getting the data, not doing the regression analysis. We told you back in, I believe, October or November, when you asked us for this, that this was a monumental job. It is a job that Dr. Wardell has taken years and years to accomplish. That kind of information cannot be obtained overnight. It took us several months to put together the information that we gave to you for 1980.

Mr. GORE. It has only been an average of, what, 15 drugs a year, something like that?

Mr. HUTT. That requires digging all kinds of places to get that information.

Mr. GORE. Three, four dates for 15 drugs a year? That's not really——

Mr. HUTT. I disagree, Mr. Gore.

Mr. GORE. But there are billions and billions of dollars involved.

Mr. HUTT. Mr. Gore, when we received the OTA data yesterday, we discovered their dates were different than our dates. There's an enormous amount of research that goes into this, in our judgment, for absolutely no useful purpose, because it does not bear upon the merits of the legislation.

Mr. **Gore**. I disagree. I think that a lot of my colleagues are going to disagree too. I think they are going to find it most unreasonable for the industry to insist on a steamroller enactment based on a mean analysis without any further look at data.

Let me yield to counsel for the minority.

Mr. **Hutt**. If I could just reply. We are not asking for a steamroller. We have provided enormous amounts of data. We have provided charts, and diagrams. We have analyzed the OTA data. In my judgment, we have shown that there is the longest regulatory review time that has ever been shown in any study coming right out of the OTA data themselves, 8.3 years. That is what this whole issue is about. It is not about the preclinical time. It is about that 8.3 years.

Mr. **Gore**. Well, that 8.3 years—and I apologize to counsel—that figure, again, is your chosen way to look at this issue, and it includes absurd examples like the Meclan example where the company itself chose, made decisions on its own to have a zero effective life.

Mr. **Hutt**. Mr. Gore, as you know, there would be zero patent restoration for Meclan.

Mr. **Gore**. But the argument upon which—I mean, the assumption on which your whole argument rests is that the mean average is this ridiculously low figure, and the way you arrive at that figure includes these ridiculous and absurd examples.

If you look at the best-selling drugs, for example, if you look at a category that excludes these exceptional cases, then the figures are very, very different. Then if you look at the effect, the practical effect of pyramided patents, if you look at the effective market share for companies even at the conclusion of the patent period, then you get a still different picture.

Mr. **Hutt**. Mr. Gore, I must respond to that. If you take a look at figure III on page 18 of our testimony, no one questions the enormous increase in the IND time as a result of the FDA pyramiding of regulatory requirements over the last 20 years. No one questions the increase in NDA approval.

Mr. **Gore**. I do. That's based on means also. That's the same tricky technique. It's also based on a mean analysis.

Mr. **Hutt**. But the bill takes that into account. The bill says if you do not lose any time to regulatory review, if your IND goes through in 1 year instead of 6, if your NDA is approved in 6 months instead of 3 years, you do not get the same amount of restoration.

The bill takes that into account. That is why all this information is so meaningless.

Mr. **Gore**. Only to a limited degree.

Let me yield to Mr. Clement, minority counsel.

Mr. **Clement**. Thank you, Mr. Chairman.

Mr. Hutt, I have to apologize. I am a lawyer, not a doctor or a clinical researcher. I may get the names wrong. What's the best selling antiulcer drug on the market now?

Mr. **Hutt**. I believe it is Tagamet. I am not a pharmacologist.

Mr. CLEMENT. That's the so-called ethical drug? It's covered by a patent?

Mr. HUTT. I believe it is.

Mr. CLEMENT. What was its effective patent life?

Mr. HUTT. I am told it is 16 years.

Mr. GORE. Will counsel yield?

Mr. CLEMENT. Certainly, Mr. Chairman.

Mr. GORE. Is it true the development costs of that drug were $40 million?

Mr. HUTT. You catch me at a disadvantage.

Mr. GORE. I believe the record will so indicate. Is it true the annual sales of that drug are now $250 million each year?

Mr. HUTT. I do not know.

Mr. GORE. I believe the record will so reflect. That's a pretty good return. Maybe that's why research and development spending has been increasing.

Mr. HUTT. The other side of that is how much money has that saved the American public and how many people have had lives saved as a result of that drug?

Mr. GORE. You know, I give the industry all the credit in the world for the figures that you cite in your statement. I am not—I don't view myself as an antagonist of this industry. [Laughter.]

I believe that it's record is a remarkable one, and I believe that it deserves better treatment in the regulatory process. That's why I have sponsored this commission and why I have tried to focus attention on ways to speed up approval, and I want to give credit where credit is due.

But I do not believe in the face of this kind of evidence where R. & D. expenditure has been increasing, innovation has not declined, a true effective patent life—that is market share and the effect of marketing practices well after the conclusion of patents being what they are in this industry—I just do not see the justification for what you are asking the Congress to do. But I have the utmost respect for the service that you have provided to the American people. I say that very sincerely.

Mr. HUTT. Mr. Gore, your point prompts me to add just one additional comment. What we don't know—and what we hope we will be able to find out—is how many more new drugs could be developed if patent restoration did indeed provide additional incentive.

You have presented information which I accept at face value from the OTA report that in real dollars as opposed to percent of sales our research and development efforts have indeed increased. That makes me feel very good. I would have liked them to increase twice as much as they in fact did.

Mr. GORE. Maybe with this new tax credit that is just taking effect you will see a further increase.

Mr. HUTT. And if we had patent restoration, it could be even more and the one drug that might solve a lot of human suffering could come out of that.

That is what we are concerned about. We want to maximize the opportunity for new drug development in this country because we do not know how we will find those drugs otherwise.

Mr. GORE. I see constituents on a regular basis who suffer when they cannot afford the medicines that are prescribed for them and at the same time meet their other expenses. So there are competing concerns.

Mr. HUTT. There are competing interests.

Mr. GORE. I am sorry, go ahead.

Mr. CLEMENT. Thank you, Mr. Chairman.

Mr. Hutt, let's take a look at a couple of other drugs. Possibly I will know more about these than my chairman will. In the past year the FDA has approved a couple of what they refer to as breakthrough drugs. Are you familiar with Blocadrin?

Mr. HUTT. I know of it. I do not know the specific details, Mr. Clement.

Mr. CLEMENT. It's a drug the FDA claims has tremendous importance to the American people because it has the ability to prevent a second heart attack. There are hundreds of millions of Americans who are subject to that.

Do you have any idea what the effective patent life is of that?

Mr. HUTT. I am sorry, I do not.

Mr. CLEMENT. It is less than 8 years.

Another drug that was approved this year was Procardia. Are you familiar with that?

Mr. HUTT. Again you are asking me details that I simply do not have available.

Mr. CLEMENT. It happens to be a drug approved for the treatment of angina. Again, it has an effective patent life of less than 8 years.

Mr. HUTT. I am not surprised, Mr. Clement, at these low effective patent lives. As Dr. Wardell has testified, the average effective patent life for the 1981 approved NCE's is 6.8 years.

Mr. CLEMENT. Is it true that this year the industry is going to spend hundreds of millions of dollars on drug research?

Mr. HUTT. Yes, indeed.

Mr. CLEMENT. Do you consider it immoral to get a reasonable rate of return on that?

Mr. HUTT. Certainly not. The real issue is how much money will there be to plow back into the development of the kind of drug you have just described 10 years from now.

Mr. CLEMENT. If there is a legitimate social goal—and I am sure the chairman would agree that there is—then subsidizing those who cannot afford drugs, the elderly, those on fixed incomes, those who are unable to afford them otherwise, and if a direct subsidy were provided, I presume the industry would support that?

Mr. HUTT. We would indeed.

Mr. CLEMENT. Let me ask you one final question.

The chairman had several comments about some of the data he would like to see. Isn't it a fact that every time anyone in the industry files for a patent, that becomes part of the public record and that record is available through the Patent Office?

Mr. HUTT. That is true.

Mr. CLEMENT. Isn't it true that every time someone files for an IND, that becomes part of the public record and is available through FDA?

Mr. HUTT. Only after the NDA is approved can you find out from FDA the IND filing date, I believe.

Mr. CLEMENT. Isn't it true from FDA you can find which ones were approved and when they were?

Mr. HUTT. After they are approved, yes.

Mr. CLEMENT. So, in fact, everything that was being asked for was already available in the public record through agencies of the Government?

Mr. HUTT. It could have been obtained through other sources. Again I would emphaize, Mr. Clement, that that is a long, arduous, detailed research job and would take months.

Mr. CLEMENT. I have no further questions, Mr. Chairman.

Mr. GORE. Do you believe if this legislation was enacted there would be an immediate increase in the amount of research and development spending?

Mr. HUTT. I do. This is a debatable point, Mr. Gore. Let me explain both sides of the issue. Some people say that the results would not be seen for 10 years because one would only then be experiencing significant patent restoration.

My experience with the pharmaceutical industry is that their investment decisions are at least in part—not totally, but in part—influenced by their perception of the American people's view of the importance of pharmaceutical innovation.

If they see the American Congress providing a better climate for innovation through patent restoration, I think they will make the investment long before that 10-year period.

Mr. GORE. It would make them feel better in general and they would want to invest more?

Mr. HUTT. It is not a question just of feeling better. They would see the likelihood of increased profits in the future through patent restoration and would factor that into their planning. There is little doubt in my mind about that. I might add other people in the industry have said exactly the same thing, including Dr. Sarett of Merck.

Mr. GORE. We were told similar increases in income for the oil industry would have certain effects, and in the steel industry as well. U.S. Steel choses not to accept that message as one that the United States was trying to tell them that we need more steel and they wanted to buy Marathon Oil instead.

Anyway, I won't belabor the point. We have run very late. It's not fair to our other witnesses to go too long. I certainly appreciate your appearance here today. In accord with the agreement that I made with the ranking minority Member earlier, we will invite you to return at the conclusion of our next presentations and join the panel.

Mr. HUTT. Thank you very much. I appreciate your hospitality.

Mr. GORE. Our next witnesses are Mr. Kenneth Larsen, president of the Generic Pharmaceutical Industry Association, Mr. Bill Haddad of the Generic Pharmaceutical Industry Association, and Alfred Engelberg with the Generic Pharmaceutical Industry Association.

STATEMENT OF KENNETH LARSEN, PRESIDENT, GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION, NEW YORK, N.Y.; ACCOMPANIED BY BILL HADDAD AND ALFRED B. ENGELBERG, ESQ.

Mr. HADDAD. Mr. Clement, before you leave, we would like to make one suggestion. We thought we heard that all the data you seek is in Dr. Wardell's computer and that he has been regularly supplied this imformation for several years. I don't know if this will help in expediting the information you requested from Mr. Hutt.

Mr. GORE. Mr. Wardell, is that in fact true that the data in question has already been provided? Could you provide that for us?

Dr. WARDELL. Mr. Gore, I did ask Mr. White whether he would like to sponsor a study by us to examine the issues. I understand there was no money.

Mr. HADDAD. I would think from my own experience, if you would permit, it would require Mr. Hutt's permission to release that confidential data. It would take, his permission to plug into that computer and a readout—my guess once having been a computer person for a number of years—it would take about 2½ hours to run that data.

Mr. HUTT. I have no authority to release that. It is the individual companies that provided the data. PMA is without authority to release any of those data.

Mr. GORE. Would you be willing to ask the individual companies if they would release it to us?

Mr. HUTT. We will certainly consider that, yes.

Mr. GORE. Could you ask them if they would release it to us?

Mr. HUTT. As I said, we will consider that, Mr. Gore. I have not thought that through. I do not want to put any pressure on the companies to release confidential data, data they regard as highly confidential.

Mr. GORE. We will come back to the panel in order to help the reporter.

Mr. HADDAD. Thank you.

Mr. GORE. We will return to that when Mr. Hutt rejoins the panel.

Who wants to go first? Mr. Larsen, please proceed.

Mr. LARSEN. If it would facilitate things, what we might do is go through all of our presentations and then respond to questions it might save time that way. I am Kenneth Larsen, chairman of the Generic Pharmaceutical Industry Association and the president and chief executive officer of Zenith Laboratories.

To provide perspective to my remarks, I have been employed in the pharmaceutical industry for 33 years, in almost every facet of the business including the FDA process, the first 30 years with a major multinational pharmaceutical company and the last 3 years with Zenith Laboratories.

Certainly I cannot help but add, Mr. Clement, that in reference to this morning's comment, I hope this qualifies me as a member of the industry.

The Generic Pharmaceutical Industry Association represents independent manufacturers and distributors of generic drugs. The member companies' generic sales represent 80 percent of the unbranded generic market. Although the companies we represent are small, by multinational pharmaceutical company standards, they are strong examples of the competitive free enterprise spirit so valued in America.

In their own localities, our companies are significant employers, with modern plants, state-of-the-art manufacturing procedures and quality control programs. Further, it is primarily through their efforts there is competition in the marketplace reducing the prices of prescription drugs. The beneficiaries are individual consumers—especially the elderly and the chronically ill—the Government and institutional purchasers of drugs.

We have been very concerned over misleading and what we regard as inaccurate statements in justification of the proposed patent extension legislation, and therefore are pleased to have this opportunity to present our views and answer your questions about effective patent life and pharmaceutical innovation.

The patent law of the United States was designed to provide a defined period of extension—17 years—in exchange for public disclosure of the invention. Issuance of a patent does not carry with it any guarantee of a fixed period of commercial exclusivity. Patents frequently issue at the idea stage, before an invention is ready to be commercially marketed and sometimes even before a commercial application of the idea has been discovered. This will be brought out more by Mr. Engelberg.

OTA made note of this fact in its report on patent term extension: "The period during the patent term in which products are marketed is usually less than 17 years because patents are obtained before products are ready to be marketed."

One would expect, therefore, that the period of protection for competition in the marketplace—what has been called effective patent life—would be less than 17 years for pharmaceuticals, as it is with other products.

Supporters of patent extension claim the effective patent life for drugs—from FDA marketing approval to the patent expiration—is only 9.5 years. We seriously question this claim.

To document, we took a look at the effective patent lives of the 12 top selling, patent-protected drugs in America. This wasn't a list we decided on. We went to recognized listings of ranked prescription drugs and determined their effective patent life. Not an easy task for a small association. What we found was the effective market patent life was not 9.5 years and not somewhat less than 17 years. The highest volume drugs in America—with U.S. sales of $1.37 billion in 1980—have an average effective patent life of 18.5 years, as can be seen up on this chart.

I thought it might be helpful to the subcommittee if we provided some additional detail on some of these products:

Zyloprim, used in the treatment of gout, covered by patent No. 3,474,098, was issued in October 1969. The first patent application, however, was filed in March of 1956. There were at least three other continuation-in-part patent applications—filed in 1960, 1962 and 1966—each superseding a previous one which we then abandoned.

The effect of continuation-in-part applications, a common practice under U.S. patent law, is no patent issues for many years—13 years in the case of Zyloprim—delaying the start of the 17-year monopoly period. As a result, Zyloprim has an effective patent life of 20 years and is a good example of how a prospective patentee can exercise significant control over when the desired patent actually issues.

We were able to identify one additional patent for Zyloprim—issued in November 1971—but we have not made a judgment as to whether this patent affords enforceable protection from competition for an additional 2 years.

Aldomet, or methyl-dopa, however you choose to identify it, with an effective patent life of 22 years, is used in the treatment of high blood pressure. In attachment B to my testimony, we have identified eight patents for this product covering a three-decade period. You will note that our chart of average market protection is based on a patent expiration date of 1984 which was confirmed in a report by the Stanford Research Institute.

I hope the subcommittee will examine this question. Also in the table, you will find the citation covering Diabinese, a drug used in the treatment of diabetes. The EPL for diabetes is 26 years. It is the longest one in the table. The patent keeps out competition that entire time. There are a number of generic companies that have approval of the product from the FDA, but are precluded from marketing it and prevented from bringing competition into the marketplace.

To avoid criticism of selectivity or limited sampling, we also examined the second group of most frequently prescribed drugs in the United States. In attachment C to my testimony, we show that average effective patent life for the combined list of 25 top-selling, patent-protected drugs is at least 16.7 years. I emphasize at least 16.7 years as there could be additional unidentified patents covering any one of these products.

I would like now to respond briefly to the subcommittee's questions concerning past and future trends in pharmaceutical innovation. This gets back to the remarks we just heard. The industry claims that innovation has declined since the 1962 efficacy amendments, and will continue to decline, these have been frequently cited as justification for extension legislation.

I think the information presented today casts a real doubt as to whether that is true or not. From my own personal experience, based upon 33 years in the industry, the number of approvals of significant new drugs in the last several months are greater than any time we have experienced in recent years.

OTA examined trends in innovation and found that the total number of new chemical entities (NCE's) increased from 136 in the 1963–71 period to 175 in the 1972 to 1980 period. This perhaps relates to some of the questions you addressed to Mr. Hutt.

The FDA reported that the number of significant new drug discoveries has remained constant ever since the fifties and regardless of the 1962 amendments. OTA supported the FDA analysis and suggested that the so-called decline in FDA approvals "involved NCE's considered to offer little or no therapeutic gain."

The evidence further indicates that the positive trend in pharmaceutical innovation is continuing, as evidenced by what occurred in 1981. OTA agreed that the factors which influence R. & D. decisions "appear to favor innovation: The industry continues to enjoy high and stable profits in terms of return to stockholder's equity; research techniques have improved; and competitive pressure for innovation has not diminished."

Regardless of past trends, all indications point to even more profitable years ahead, without the benefits of patent extension. The New York Times reported in an article entitled "The Drug Business Sees a Golden Era Ahead," that the industry anticipates enormous profits from the heavy R. & D. expenditures it has been making and plans to make.

OTA found that research-intensive companies are committing increasing amounts of funds toward pharmaceutical R. & D. Wall Street agrees. An analysis by Morgan Stanley & Co., attached to my testimony as appendix E, reported:

> There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced.

Innovation is, of course, essential to our national well-being and should be encouraged. Our own industry depends in large measure on the basic R. & D. work of the major companies.

Equally important, however, is the availability of affordable medicine. Even now, without extended patent terms, the American Association of Retired Persons reports that some 70 to 75 percent of drug misuse among the elderly is due to underutilization because they cannot afford the medicine that has been prescribed.

I want to add, last week Mr. Engman and I were privileged to appear before the combined council of the American Association of Retired People and the National Retired Teachers Association. The group had taken a position favoring patent extension.

It is my understanding that following our appearances—the associations elected to withdraw their support as a result of their concern about health-care costs.

No one to date has been able to measure the effectiveness of patent extension on innovation, whereas the effects on the drug prices and on individual consumers has been documented. The OTA concluded, consumers will pay more for most drugs. OTA reported:

> Furthermore, some groups of consumers, the elderly and chronically ill, will be disproportionately affected, and these groups may be less capable than the population as a whole of bearing the increased costs.

Just as we should do all we can to encourage the development of vital new drugs, so must we also do all in our power to improve competition and reduce costs. Legislation which AARP concludes "will result in very real income transfers from elderly consumers to large brand name manufacturers" does not accomplish this objective.

On this basis, we can only conclude that new chemical entity drug approval has not been adversely affected and the market protected life of drugs is reasonable.

I want to comment further as one who manages a business and one who has been involved in this industry for a great number of years, that it is my personal observation and belief that the 25-percent tax credit incentive will support increased R. & D. I know in my own company it has redirected our attention toward this opportunity. We intend to take advantage of it. We intend to move drugs up faster than we would have been able to do in the past.

I think that a solution is needed to this problem and it is my own personal belief and not totally supported by the organization which I represent that we could agree to some period of guaranteed patent protection period from the date of FDA submission, subject to a part of an overall settlement of a variety of issues relating to barriers to pharmaceutical competition such as sizes, shape, and color, the pyramiding of patents that have been put forth in some of the earlier discussions, and FDA processing of generics.

I would add a caveat in the case that if a drug does not receive NDA approval within 5 years of the date of issuance of the patent, that then it would revert back to the original patent date and no further consideration would be given.

I have looked at the lists of drugs introduced this morning. I am concerned about the amount of discretionary time in that IND process that is available to companies. I know the companies, if they have two drugs coming out of research for the same indication, they are going to back one with the highest probability of success. Secondary support will go to the lower probability drug.

I think there is an opportunity to build a good bill, a bill that can serve the interests of the people, and you know at the heart of this issue is what is a reasonable period of market-protected life and the means by which it can be achieved.

The actual time being taken by the FDA in the regulatory review is a relatively minor part; 2 years I guess is what we could all agree on. Certainly on the basis of Dr. Hayes' comments we can expect even tighter and more effective control that there will improve on the time required.

But what can be done? I guess from my own vantage point and in conclusion, if the members of this committee were to seek out improvements in the bill, I would encourage you to get the parties together that have the greatest interest in the bill. I discussed this with Mr. Engman. He indicated to me as late as last week that he would be willing to sit down and talk about changes to the bill.

I encourage the committee to provide the form and leadership that would bring the parties together to build the most effective piece of legislation to accomplish the desired objectives.

With that, I would like to close and turn to Mr. Engelberg.

[The statement of Mr. Larsen follows:]

STATEMENT OF KENNETH N. LARSEN, CHAIRMAN, GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION

My name is Kenneth N Larsen. I am Chairman of the Generic Pharmaceutical Industry Association ('GPIA") and the President and Chief Executive Officer of Zenith Laboratories. To provide perspective to my remarks, I have been employed in the pharmaceutical industry for thirty-three years—the first thirty with a major, multinational pharmaceutical company and the last three with Zenith Laboratories.

The Generic Pharmaceutical Industry Association represents independent manufacturers and distributors of generic drugs. The member companies' generic sales represent 80 percent of the unbranded generic market. Although the companies we represent are small by multinational pharmaceutical company standards, they are strong examples of the competitive free enterprise spirit so valued in America. In their own localities, our companies are significant employers, with modern plants, state-of-the-art manufacturing procedures and quality control progams. Further, it is primarily through their efforts there is competition in the marketplace reducing the prices of prescription drugs. The beneficiaries are individual consumers—especially the elderly and the chronically ill—the government and institutional purchasers of drugs.

We have been very concerned over misleading and what we regard as inaccurate statements in justification of the proposed patent extension legislation, and therefore are pleased to have this opportunity to present our views and answer your questions about effective patent life and pharmaceutical innovation.

The patent law of the United States was designed to provide a defined period of extension—17 years—in exchange for public disclosure of the invention. Issuance of a patent does not carry with it any guarantee of a fixed period of commercial exclusivity. Patents frequently issue at the "idea" stage, before an invention is ready to be commercially marketed and sometimes even before a commercial application of the idea has been discovered. OTA made note of this fact in its report on Patent Term Extension: ". . . the period during the patent term in which products are marketed is usually less than 17 years because patents are obtained before products are ready to be marketed."

One would expect, therefore, that the period of protection for competition in the marketplace—what has been called Effective Patent Life—would be less than 17 years for pharmaceutical, as it is with other products.

Supporters of patent extension claim the Effective Patent Life for drugs—from FDA marketing approval to patent expiration—is only 9.5 years. We seriously question this claim.

To document, we took a look at the effective patent lives of the 12 top-selling, patent-protected drugs in America, not any easy task for a small Association. We we found was the Effective Patent Life (EPL) was not 9.5 years and not somewhat less than 17 years. The highest volume drugs in America—with U.S. sales of $1.37 billion in 1980—have an average effective patent life of 18.5 years.

I thought it might be helpful to the Subcommittee if we provided some additional detail on some of these products:

Zyloprim used in the treatment of gout, covered by Patent No. 3,474,098 was issued in October 1969. The first patent application, however, was filed in March of 1956. There were at least 3 other continuation-in-part patent applications—filed in 1960, 1962 and 1966—each superceding a previous one which was then abandoned.

The effect of continuation-in-part applications, a common practice under U.S. patent law, is no patent issues for many years—13 years in the case of Zyloprim—delaying the start of the 17-year monopoly period. As a result, Zyloprim has an effective patent life of 20 years and is a good example of how a prospective patentee can exercise significant control over when the desired patent actually issues.

We are able to identify one additional patent for Zyloprim—issued in November 1971—but we have not made a judgement as to whether this patent affords enforceable protection from competition for an additional 2 years.

Aldomet, with an effective patent life of 22 years, is used in the treatment of high blood pressure. In Attachment "B" to my testimony, we have identified 8 patents for this product covering a three decade period. You will note that our chart of average market protection is based on a patent expiration date of 1984 which was confirmed in a report by the Stanford Research Institute. The subsequent patents on Aldomet may or may not extend market protection beyond 1984, and I hope the Subcommittee will examine these questions. Please also note that Aldoril, which is Adlomet with Hydrochlorothiazide, may also be protected by the small patents.

Also in Attachment "B" you will find citations for patents covering Diabinese, a drug used in the treatment of diabetes. The EPL for Diabinese—the 26 year period of patent life keeps out competition and forces consumers and the government to pay monopolistic controlled prices.

To avoid criticism of selectivity or limited sampling, we also examined the second group of most frequently prescribed drugs in the U.S. In Attachment "C" to my testimony, we show that average effective patent life for the combined list of 25 top-selling, patent-protected drugs is at least 16.7 years. I emphasize "at least" 16.7 years as there could be additional unidentified patents covering any one of these products.

I would like now to respond briefly to the Subcommittee's questions concerning past and future trends in pharmaceutical innovation. The industry's claims that innovation has declined since the 1962 efficacy amendments, and will continue to decline, have been cited frequently as another justification for extension legislation.

We question both of these claims.

OTA examined trends in innovation and found that the total number of new chemical entities (NCEs) increased from 136 in the 1963–1971 period to 175 in the 1972 to 1980 period.

The FDA has reported that the number of significant new drug discoveries has remained constant ever since the 1950's and regardless of the 1962 amendments. OTA supported the FDA analysis and suggested that the so-called decline in FDA approvals "involved NCEs considered to offer little or no therapeutic gain."

The evidence further indicates that the positive trend in pharmaceutical innovation is continuing.

OTA agreed that the factors which influence R&D decisions "appear to favor innovation: the industry continues to enjoy high and stable profits in terms of return to stockholder's equity; research techniques have improved; and competitive pressure for innovaction has not diminished."

Regardless of past trends, all indications point to even more profitable years ahead, without the benefits of patent extension. The New York Times reported in an article entitled "The Drug Business Sees a Golden Era Ahead," that the industry anticipates enormous profits from the heavy R&D expenditutes it has been making and plans to make.

OTA found that "research-intensive companies are committing increasing amounts of funds toward pharmaceutical R&D.

Wall Street agrees. An analysis by Morgan Stanley & Company attached to my testimony as Appendix "E" reported: "There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced."

Innovation is, of course, essential to our national well being and should be encouraged. Our own industry depends in large measure on the basic R&D work of the major companies.

Equally important, however, is the availability of affordable medicine. Even now, without extended patent terms, the American Association of Retired Persons reports that some 70 to 75 percent of drug misuse among the elderly is due to under-utilization because they cannot afford the medicine that has been prescribed.

While no one to date has been able to measure the effect of patent-extension on innovation, the effects on the drug prices and on individual consumers has been documented. The OTA concluded, consumers will pay more for most drugs. "Furthermore," OTA reported, "some groups of consumers, the elderly and chronically ill, will be disproportionately affected, and these groups may be less capable than the population as a whole of bearing the increased costs."

Just as we should do all we can to encourage the development of vital new drugs, so must we also do all in our power to improve competition and reduce costs. Legislation which AARP concludes "will result in very real income transfers from elderly consumers to large brand name manufacturers" does not accomplish this objective.

On this basis we can only conclude that new chemical entity drug approval has not been adversely effected and the market protected patent life of drugs is reasonable.

We would agree to a guaranteed patent protection period of 17 years from the date of NDA submission for drugs provided the added coverage currently available through process and use patents is set aside. An added caveat would be NDA submissions would have to be made to the FDA within 5 years of the date of the issuance of the patent otherwise the protection period would revert to the date the patent issues.

This we believe is a fair and reasonable approach. It provides an adequate period for a company to recover their development costs and generate earnings to support the companies overall vitality while protecting the consumers and government interests for lower cost effective drugs.

ATTACHMENT "A"

Generic Pharmaceutical Industry Association

600 Third Avenue, 18th Floor
New York, New York 10016
Telephone (212) 490-8028

FACT SHEET ON PATENT EXTENSION (H.R. 1937)

- The top selling drugs in America are realizing actual legal patent protection for an average of 18.5 years. (See page 2)
- The U.S. pharmaceutical industry is one of the most profitable of all manufacturing industries and "continues to enjoy high and stable profits in terms of return to stockholders' equity."
- "Revenues of the pharmaceutical industry have increased steadily and the relationship between revenues and R&D expenditures has remained stable."
- "Research-intensive companies are committing increasing amounts of funds toward pharmaceutical R&D, and therefore, the potential exists for major pharmaceutical discoveries."
- The Administration is committed to reducing unnecessary regulatory requirements. FDA is already trying to expedite its approval of new drugs and "the duration of the drug approval process may therefore stabilize."
- Patent extension will delay competition and deprive consumers and government purchasers of the savings they can realize with identical, but lower-priced generic drugs.
- The costs of patent extension will fall heaviest on young and middle income families, on the nation's elderly and the chronically ill.
- The benefits of patent extension "will accrue to a few firms" which are already among the most profitable multinational companies in the world.
- The evidence available "neither supports nor refutes the position that innovation will increase significantly because of patent term extension."

NOTE: All quotes are from Patent Term Extension and the Pharmaceutical Industry, Office of Technology Assessment, Congress of the United States. 1981.

Drug Patents Exceed the Statutory Maximum

The stated rationale for patent extension legislation (HR 1937) -- that the federal regulatory process has reduced effective patent life for pharmaceutical products to only 9.5 years -- is not supported by the facts.

The U.S. patent holders of the most frequently prescribed drugs in America, with annual sales of $1,371,000,000, are realizing legal patent protection for an average of 18.5 years

DRUG PRODUCT	1980 SALES* (millions)	NDA APPROVAL	PATENT EXPIRATION	YRS. MARKET PROTECTION
Tagamet (Cimetridine)	$233	1977	1993	16
Valium (Diazepam)	220	1963	1985	22
Inderal (Propranolol)	179	1967	1984	17
** Aldomet (Methyldopa)	133	1962	1984	22
Keflex (Cephalexin)	131	1971	1987	16
Clinoril (Sulindac)	115	1978	1989	11
Indocin (Indomethacin)	75	1965	1981	16
Naprosyn (Naproxen)	75	1976	1989	13
Aldoril (Methyldopa w/ Hydrochlorothiazide)	58	1962	1981	19
Diabinese (Chlorpropamide)	53	1958	1984	26
Mellaril (Thioridazine)	50	1959	1983	24
Zyloprim (Allopurinal)	49	1966	1986	20

AVERAGE YEARS OF MARKET PROTECTION: 18.5

Total Sales Volume, 1980: $1,371,000,000

* IMS DATA

**Motrin, the 4th ranking drug in America, is licensed by the British patent holder to a U.S. company.

The Pyramiding of Drug Patents

The claim that prescription drugs realize only 9.5 years of patent protection is based on a four-page magazine summary * of an analysis which is seriously flawed in methodology: the authors calculate effective patent life by measuring from the date of the earliest patent issued. Their analysis does not take into account the pyramiding effect of subsequent use, process, or other patents which extend patent terms and prolong monopoly life and premium pricing of prescription drugs.

The authors of this much-quoted article have further understated actual patent life of pharmaceuticals by limiting their analysis to New Chemical Entities (NCEs) and excluding all other drug products. OTA acknowledges this flaw in its report on patent extension.

> "By focusing on NCEs, the most extreme reductions in effective patent terms can be determined, but these effects are not representative of the average effects for all new pharmaceuticals."

It should also be noted that while the four-page magazine article has been cited as the basic -- if not sole -- justification for patent term extension, the full analysis is not yet issued, has not been submitted to the sponsoring agency for review, and is not available for independent verification.

* Research Management, January 1981. "The Decline in Effective Patent Life of New Drugs," a four-page article by Martin M. Eisman & William M. Wardell.

Is Innovation Declining?

Another underlying premise of the pending patent extension legislation -- that pharmaceutical innovation is declining -- is not supported by the findings of the Office of Technology Assessment:

- "Competitive pressure for innovation has not diminished."
- "The relationship between revenues and R&D expenditures has remained highly stable over the past 15 years."
- "Many research intensive firms have indicated that they are increasing R&D expenditures."

Although the number of NCE approvals is an incomplete measurement of innovation, OTA uses this method to determine trends in the industry. Data provided OTA by the Food and Drug Administration shows that the number of NCEs approved in the 8-year period from 1972 to 1980 increased significantly over the number approved in the previous 8-year period:

APPROVED NCEs

	1963 to 1971	1972 to 1980
Totals:	136	175

More importantly, OTA found that "approvals of NCEs offering important or modest therapeutic gain have remained relatively stable."

The Costs and Benefits of Patent Extension

"The price of drugs whose patents are extended will be higher during the extended period than they would have been if patent protection ended." *

"Competitive pressures on patented drugs from generically equivalent drugs will be delayed and in some cases prevented by patent-term extension." *

Since 84% of prescription drug purchases are paid by consumers and not by third-party reimbursement programs, the additional costs of patent extension will fall heaviest on the elderly, the chronically ill, and on young and middle income families. **

* OTA Report.

**See comparative prices and projected annual savings that can be realized with identical generic products, pg. 8.

"The bulk of revenues generated by patent-term extension will accrue to a few firms who have developed financially successful drugs." *

The American Association of Retired Persons and the National Retired Teachers Association summarized the cost/benefit relationship of patent extension in a statement submitted to the Senate Judiciary Committee: **

> "We can be sure that additional years of patent protection will result in very real income transfers from elderly consumers to large brand-name manufacturers."

While the Report of the Senate Judiciary Committee made note of the support from AARP/NRTA of "the concept of patent restoration," it failed to cite the Associations' expressed concerns and recommendation:

> "Enactment of patent restoration will likely result in additional increases in the elderly's expenditures for prescription drugs."
>
> "We are concerned about the effect patent restoration would have on competition in the drug industry, particularly price competition, and whether the benefits of patent term restoration are commensurate with the costs such legislation would necessarily entail."
>
> "Finally, our Associations recommend that alternative approaches to further drug research, development and innovation be explored with the aim being to find alternatives to prescription drug prices as a means of financing R&D."

* OTA Report.

** Statement of the National Retired Teachers Association and the American Association of Retired Persons on S.255, the Patent Term Restoration Act of 1981, Submitted to the Committee on the Judiciary, United States Senate, April 30, 1981.

The Case for Patent Extension - Fact or Fiction?

The arguments for patent extension are based, according to OTA, on "a widespread belief" that the return to R&D investment is declining.

OTA, however, finds that there is not sufficient data to prove the accuracy of this widespread belief, and concludes:

> "Many factors that influence R&D decisions appear to favor innovation: the industry continues to enjoy high and stable profits in terms of return to stockholder's equity; research techniques have improved; and competitive pressure for innovation has not diminished."

The "problems" which HR 1937 is supposed to remedy may in fact, therefore, not really exist:

- Drug products, as shown, frequently have effective patent lives in excess of the 17-year statutory maximum.
- "The duration of the FDA regulatory procedures may be stabilizing" according to OTA, and the Agency "is now giving highest priority to the drugs that it believes will provide significant therapeutic advances. . ."
- "Pharmaceutical companies earned the fourth highest return on equity in American industry last year, at 20.5 percent, ranking behind the oil services industry, energy companies and the tobacco industry." *
- "There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced." **

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* The New York Times, "The Drug Business Sees a Golden Era Ahead," May 17, 1981.

** Medical Marketing and Media. "The Drugs in the Eighties: The Growth will be There-Part I," August 1981.

The Generic Drug Industry

Competition from the generic drug industry has significantly reduced the cost of prescription medicine.

The Federal Trade Commission estimated in 1979 that "between 42.1 percent and 74.3 percent of the wholesale price of branded drugs could be saved by the dispensing of nonbranded products instead of more expensive branded drugs." *

For the nation's elderly, who pay 25 percent of the national drug bill, price competition can be a life or death matter. Some 70 to 75 percent of drug misuse among the elderly is due to under-utilization because they cannot afford the medicine that has been prescribed.

Despite the savings that can be realized by the use of identical, but lower-priced generic drugs, 80 to 85 percent of the drugs having generic competition are sold by the large pharmaceutical companies.

Even after patents expire, branded products enjoy what OTA calls "post patent exclusivity," a further extension of market share and monopoly pricing. One study cited by OTA showed that after patents expired, each of 12 major drugs (including Librium and Darvon) retained more than a 90 percent share of the drugstore market and more than an 80 percent share of the hospital market.

Patent extension will provide additional opportunities to extend monopoly pricing periods beyond the 17-year statutory patent term. The members of the GPIA believe that patent extension will delay or preclude the entry of generic drugs into the market, eliminate the competition they provide, and force consumers and government purchasers to pay higher prices for prescription drugs.

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* OTA Report.

COMPARATIVE GENERIC/BRAND NAME DRUG PRICES

Generic (Brand Name) Drug Products	Generic* Price	Brand* Price	Brand Price Times Greater	Annual** Brand Drug Expenditures (millions)	Equivalent Generic Cost (Col.5 ÷ Col.4) (millions)	Possible Generic Savings (Col.5 - Col.6) (millions)
Dipyridamole (Persantine) 25 mg./1000s	$23.75	$108.34	4.6	$58,937	$12,812	$46,125
Isosorbide Dinitrate (Isordil) 5 mg./100s sublingual	1.46	5.41	3.7	54,102	14,622	39,480
Amitriptyline HCL (Elavil) 25 mg./1000s	17.71	73.53	4.2	29,613	7,051	22,562
Chlordiazepoxide HCL (Librium) 10 mg./500s	5.63	43.65	7.8	27,675	3,548	24,127
Tolbutamide (Orinase) 0.5 gm./1000s	42.67	91.58	2.2	22,637	10,290	12,347
Hydralazine HCL (Apresoline) 25 mg./1000s	11.74	66.07	5.6	22,441	4,007	18,434
Isoxsuprine HCL (Vasodilan) 10 mg./1000s	22.72	137.74	6.1	19,101	3,131	15,970
Meclizine HCL (Antivert) 12.5 mg./1000s	8.73	61.76	7.1	17,173	2,419	14,754

TOTAL POSSIBLE GENERIC SAVINGS: $193,799,000

* 1981 Redbook Prices
**1980 IMS Data

APPENDIX "B"

Drug Product	Patent Number	Issue Date	Expiration Date
Aldomet	2,868,818	1959	1976
	3,158,648	1964	1981
	3,230,143	1966	1983
	3,344,023	1967	1984
	3,347,752	1967	1984
	3,517,057	1970	1987
	3,526,698	1970	1987
	4,038,411	1977	1994
Diabinese	3,013,072	1961	1978
	3,121,102	1964	1981
	3,211,615	1965	1982
	3,349,124	1967	1984

APPENDIX "C"

MARKET PROTECTION OF DRUG PRODUCTS

Drug Product	1980 Sales (millions)	NDA Approval	Patent Expiration	Years of Market Protection
Dalmane	$47	1970	1989	19
Ovral	$47	1968	1982	14
Timoptic	$45	1978	1988	10
Tranxene	$40	1972	1987	15
Minipress	$38	1976	1987	11
Haldol	$35	1967	1986	19
Sinequan	$35	1969	1986	17
Nalfon	$32	1976	1988	12
Talwin	$30	1962	1983	21
Ativan	$29	1977	1986	9
Catapres	$25	1965	1982	17
Bactrim DS	$23	1978	1993	15
Valisone	$21	1967	1984	17
13 products	$447			15.1 average years
Top 25 drugs	$1,818			16.7 average years

THE NEW YORK TIMES
May 17, 1981

APPENDIX "D"

The Drug Business Sees A Golden Era Ahead

Hit on a Tagamet, and the money rolls in. New funds are pouring into research. Do science and Reagan spell an end to 'drug lag'?

BY THOMAS C. HAYES

THE Warner-Lambert Company, a major pharmaceutical concern, earned a respectable 13.3 percent on shareholder investment last year, just a shade below the national average for manufacturers of all stripes. But in the exceptionally profitable pharmaceutical industry, it was an also-ran.

Warner-Lambert and its fellow also-rans now have a chance to recoup. With the expectation of increasing demand for a host of new drugs for an aging population, with early signals that the Reagan Administration will relax regulatory requirements, and with such dramatic advances as interferon research in the biological sciences, the drug industry may be on the brink of even greater profitability.

"These factors will make the 1980's a golden age of drug research," Ronald M. Nordmann, senior drug analyst at Oppenheimer & Company, said. "You will see more interesting new drugs in the 1980's than any decade within memory."

This is the industry of the Big Breakthrough, where the introduction of one successful product can literally make a faltering company whole or pay for an expensive research program many times over. No one knows this better than the SmithKline Corporation, whose stock has multiplied eightfold since 1975, the year before its ulcer remedy, Tagamet, was introduced. Profits from Tagamet, which last year passed Valium as the world's largest-selling prescribed drug, have helped catapult SmithKline into the big-spending race to create new cures.

The drug manufacturers, in addition to seeking speedier Government testing, are already lobbying for extension of drug patents to hold on longer to exclusive rights on best-selling drugs. And virtually all of them are planning higher outlays for research.

In the 70's, companies like Warner-Lambert suffered by comparison because they were slow to commit funds to aggressive research. "We have not had the most productive history in developing new compounds," Donald E. O'Neill, president of Warner's Parke-Davis pharmaceutical division, acknowledged in an interview.

This year, though, reflecting an outlook that has become close to gospel across the pharmaceutical business, Warner allocated about $80 million of its overall $120 million research budget to Parke-Davis. The 20 percent increase is typical of big and small companies alike. Warner, meanwhile, is hoping to strike it rich with Lopid, a hypertension drug awaiting approval from the Food and Drug Administration. A success with Lopid would bring in large amounts of cash that could further support research.

Best-selling drugs like Tagamet can tally $5 billion in sales in 10 years on an investment of roughly $40 million. Such discoveries can transform a dull, frustrated company into the envy of its peers.

"The name of the game continues to be getting the big product to come along and have an important effect on sales and earnings," Neil P. Sweig, health care analyst with Shearson Loeb Rhoades Inc., said.

Companies are using advances in molecular biology and computer science to concentrate their research on drugs that have a wide potential application. Before, research was more of a hit-or-miss screening of unproven compounds. Today, the biggest efforts are being mounted for drugs to treat heart disease, hypertension or high blood pressure, arthritis and the varieties of aches and pains associated with advancing age.

Restrictions by the F.D.A. have continually narrowed the number of new drugs approved each year. Under the Reagan Administration, a general move toward deregulation is expected. No one, however, is predicting a return to the days before 1963 when drug manufacturers had only to establish that a new drug was safe before it was approved for general use by physicians. Since then, manufacturers have also had to prove that their new drugs actually worked. From a high-water mark of 65 new drug introductions in 1959, the figure dropped to 12 last year. Top researchers in the major drug companies, like Merck & Company, Pfizer Inc. and Eli Lilly & Company, and industry analysts are reluctant to say how much they expect the so-called drug lag to abate. Most believe it will.

"People have seen the importance of new products and their specific, positive effect on human health," said Dr. P. Roy Vagelos, a physician who heads Merck & Company's research arm, Merck Sharp & Dohme Research Laboratories. "It's also fair to say there will be a significant increase in new drugs because of what has happened in science," he added.

THE drug companies were once tight-lipped about the secret compounds still submerged in a battery of animal and patient tests mandated by the F.D.A. Today, by contrast, they are more eager to discuss the potential of the drugs. The bidding on Wall Street for pharmaceutical shares is closely tied to the promise of drugs in the pipeline.

"Stocks move on the basis of significant new products," John P. Curran, a specialist in pharmaceutical economics at Wood Gundy, said. "A stock will explode on news of big prescriptions after a new drug is introduced."

Merck created a stir on April 1 when it announced that a new drug, Timolol, reduced deaths among 188 patients who had suffered recent heart attacks by 39 percent. The company's shares jumped 4⅝, to 89½, that day, and subsequently reached 96⅝, closing Friday at 93, up 2⅝.

Another Merck offering, Heptavax-B, "has the potential to eradicate hepatitis B virus infections, which is uncurable and untreatable, much like measles has been eradicated," Dr. Vagelos said. Both drugs have completed pre-market tests. Merck hopes to manufacture them for sale next year if the F.D.A. approves the drugs.

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Merck, with headquarters in Rahway, N.J., is spending $280 million on research this year, the most of any American pharmaceutical manufacturer. It was the most profitable, earning $415.4 million, with a hefty 13.3 percent profit margin and 22.3 percent return on equity.

"Merck has always been the premiere research house in the United States," Mr. Nordmann of Oppenheimer said. "But it went through a very dry period, from 1965 to 1975. It now appears they are back on stream with an overabundance of new products that are about to be introduced."

Although Merck might have appeared dormant, it did not cut back on research, according to Dr. Vagelos. "Many of the drugs that are breaking the surface now were in the pipeline during that time," he said.

It's true that a company never knows when research will be successful. "But, as these biological processes are elucidated better and better," said Marsha H. Fanucci of Arthur D. Little Inc., a consulting concern, "it will allow companies to be more technologically and philosophically sophisticated."

The first signs are already apparent, research executives say. "The main impact of the new biology is making itself felt now at earlier stages of investigation for new compounds," Dr. Barry M. Bloom, head of research at Pfizer, said.

As an illustration, Dr. Bloom said Pfizer researchers were able to use gene-splicing methods to quickly identify a drug that appears to sharply reduce deterioration of the nervous sytem suffered by people with severe cases of diabetes.

It took Pfizer three years to identify the compound and another two years for preliminary tests in humans. "I wouldn't want to guess how long it would have taken by random, nonrational searching," Dr. Bloom said. The drug, Sorbinil, was patented in December 1978. Pfizer must complete another study of the drug's effect on dozens of patients before it can apply for F.D.A. approval.

At the end of 1980, it took a drug manufacturer an average of 33 months to obtain approval from the F.D.A. to begin selling a new drug. Pfizer, for instance, has been waiting since March 1978, for approval of Feldene, a once-a-day treatment for arthritis. The drug has been a success in several European countries. Analysts who follow Pfizer expect that Feldene's worldwide sales could eventually top $200 million a year after it is approved in this country.

THE F.D.A. is a unit of the Department of Health and Human Services. It has come under fire from drug manufacturers, who contend that the agency too often drags its feet before completing its review of a new drug application. But the long and expensive path to marketing a drug cuts both ways. Companies with F.D.A. approval to sell a drug have a strong edge over competitors seeking to sell a copy or a slight variation of their innovative drug.

Critics of the pharmaceutical research companies say that keeps drug prices artificially high and unjustly inflates profits. In response to those pressures, the Reagan Administration last month opened the door for the F.D.A. to allow so-called "me-too" manufacturers to cite published tests of the pioneering research companies in compiling their applications, rather than being forced to replicate the costly experiments on their own.

Still, Richard S. Schweiker, the new Secretary of Health and Human Services, is expected to trim the so-called drug lag at the F.D.A. The new head of the F.D.A., Dr. Arthur Hull Hayes Jr., a physician from Pennsylvania, was chosen by Mr. Schweiker. Members of the Reagan Administration are well-acquainted with the drug manufacturers' laments. Mr. Schweiker was an active author of legislation to ease drug regulations when he was a Republican Senator from Pennsylvania.

"The appointment of Schweiker is a big plus for the drug industry," Mr. Nordmann of Oppenheimer, said. "His goal is to eradicate the drug lag. It will cut down on the time and expense of getting a new drug on the market."

Vice President Bush was a director of Eli Lilly from 1977 to 1979. And Donald H. Rumsfeld, Secretary of Defense in the Ford Administration, is now president and chief executive of the G.D. Searle Company. The F.D.A. has blocked Searle's introduction of a putatively profitable, noncaloric sweetener called Aspartame, since 1974, requiring more tests on possible harmful side effects.

In addition to more expeditious drug reviews, drug manufacturers are seeking extension of patent laws that would guarantee them certain years of exclusive manufacturing and marketing rights for the drugs they develop in their laboratories.

According to the Pharmaceutical Manufacturers Association, the 12 drugs approved in 1980 averaged 10 years in research and F.D.A. review before they could be sold. That left seven years of exclusive sales rights. After that, competing manufacturers will be free to study the research and sell copies of the original drug.

Dr. Sidney Wolfe, a physician who heads the health care unit of Public Citizen, a consumerist lobbying group in Washington, contends that Americans have paid too high a price for prescription drugs. The United States is one of the few countries in which the government does not control the price of drugs.

"It's an industry that is rolling in money," Dr. Wolfe said. He also attacked efforts by pharmaceutical companies to convince Congress to extend drug patents. The manufacturers argue that they are increasingly less able to recoup their research costs, because of the dwindling patent life.

"It's outrageous," Dr. Wolfe countered. "The best-selling drugs have hit as much as $5 billion in sales before the patents come off. Their research is not terribly creative anyway. Most drugs are copies of what is already available. They offer little therapeutic advantage."

In brief, the debate is over how much profit is enough for drug manufacturers, given the risks they assume. They do not publish profit markups on the drugs they sell. But Dr. Wolfe contends that it is not unusual for pioneering drugs to sell at wholesale for seven times the price of generic copies.

"That should give you an idea of the fraction of the wholesale price that is represented by actual cost, including research and development," he said. Drug executives argue that the threat of lawsuits hangs over each of their products, despite what could be an experience of thousands of prescriptions without damaging side effects.

The Pharmaceutical Manufacturers Association, adding the average expense of research gone awry on laboratory failures, puts the average cost of marketing new drugs at $70 million. The risks of unfore-

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seen side effects and related vulnerabilities to law suits add to a drug company's expenses. Last year, for instance, SmithKline pulled a new antihypertension drug from the market after reports of liver disorders and some deaths. It has been hit by 30 law suits. The drug, Selacryn, was licensed from a French manufacturer.

Despite such vagaries, pharmaceutical companies earned the fourth-highest return on equity in American industry last year, at 20.5 percent, ranking behind the oil services industry, energy companies and the tobacco industry.

Breakthrough drugs contribute most of the profits. Four out of five drugs available never cross the threshold of sales of $20 million a year, according to the Arthur D. Little firm. In some cases, the huge investments and long seed time necessary to execute a successful research program have caused some companies to back away from drugs, according to Richard L. Hughes, a health-care specialist with Little.

"One group says that even if you bring out a wonder drug in 10 years, it may not equal what you could get by simply investing in the money market at 15 percent and waiting 10 years," he said. "Risk and return has become a very important factor."

In the main, however, drug company executives are going with the scientists, putting more money into research today with the hope that more new drugs and bigger profits will blossom at some distant tomorrow.

"All it takes is one hit every three to five years, and you can sustain all the risk," Mr. Sweig, the Shearson analyst, said. ■

NO. 2: **VALIUM**

Valium is no longer the runaway leader among prescription drugs, but the tranquilizer and muscle-relaxant still is among the world's most widely dispensed druggist potions.

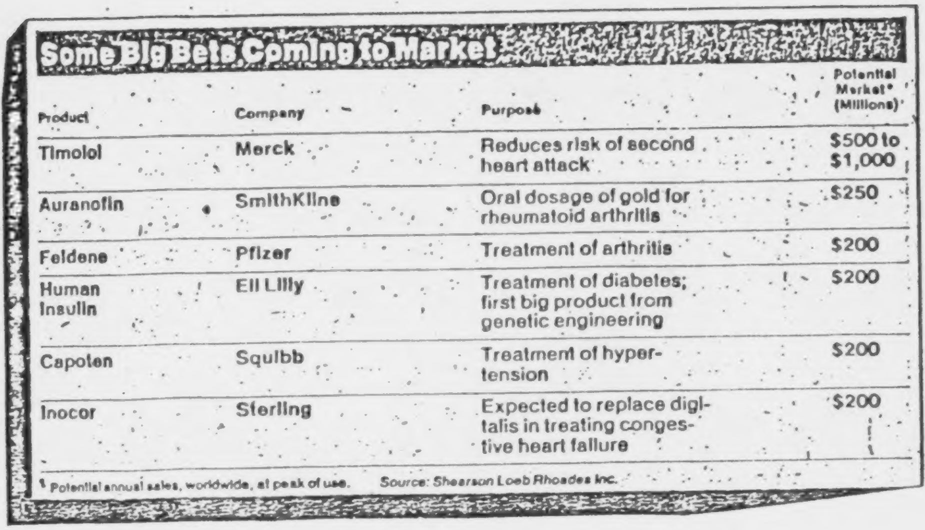
Valium rang up about $350 million in sales around the world last year for its creator, Hoffman-La Roche Inc. That trailed the $625 million for Tagamet, the five-year-old ulcer treatment from the SmithKline Corporation.

From a peak of more than 50 million in 1975, Valium prescriptions dipped below 33 million last year. Physicians have been disturbed by patient abuse of the drug, especially when combined with alcohol. Some heavy users also have suffered addiction. The company maintains that Valium's safety under proper dosage has never been in dispute.

A further dip in sales is expected after 1985, when Valium's patent expires. "Valium is being looked at enviously by a number of people," Irwin Lerner, president and chief executive of Hoffman-LaRoche, said in an interview at the company's American headquarters, in Nutley, N.J. The company, which posted $2.5 billion in worldwide sales last year, is based in Basel, Switzerland.

Still, Hoffman-LaRoche has had a huge and steady stream of profits from Valium since its introduction in 1963. It helped bankroll the company's strong position among the small army of companies searching for new drugs, including a cancer cure from an interferon compound. Roche poured $350 million into research last year, the most of any drug company in the world.

"The profits from Valium are footing the bill for our work in interferon," Mr. Lerner said. "We think we have more exciting leads than at any other time in our history."



Some Big Bets Coming to Market

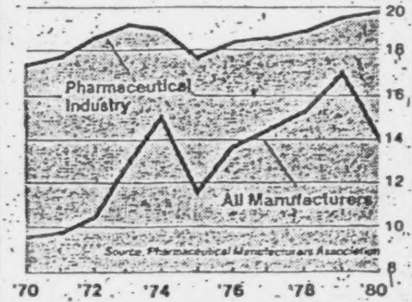
Product	Company	Purpose	Potential Market[*] (Millions)
Timolol	Merck	Reduces risk of second heart attack	$500 to $1,000
Auranofin	SmithKline	Oral dosage of gold for rheumatoid arthritis	$250
Feldene	Pfizer	Treatment of arthritis	$200
Human Insulin	Eli Lilly	Treatment of diabetes; first big product from genetic engineering	$200
Capoten	Squibb	Treatment of hypertension	$200
Inocor	Sterling	Expected to replace digitalis in treating congestive heart failure	$200

[*] Potential annual sales, worldwide, at peak of use. Source: Shearson Loeb Rhoades Inc.

A Prescription for Profit

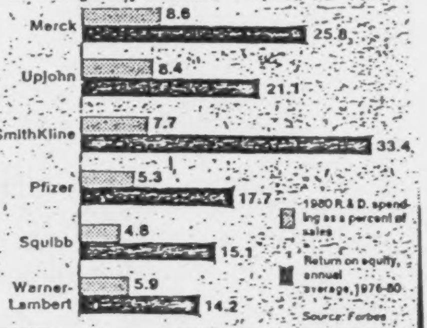
Profitability has consistently been good.

Return on equity, in percent



Source: Pharmaceutical Manufacturers Association

Research is considered the key to profits.



Source: Forbes

The Top Sellers

Ranked by 1980 sales in the United States

Drug	Manufacturer	Disease or Function	Introduced	Sales (Millions)
Tagamet	SmithKline	Peptic ulcers	1977	$250
Valium	Hoffmann-LaRoche	Muscle relaxant, tranquilizer	1966	$230
Inderal	Am. Home Products	Heart disease, hypertension	1967	$200
Motrin	Upjohn	Arthritis	1974	$150
Aldomet	Merck	Hypertension	1963	$150
Dyazide	SmithKline	Hypertension	1965	$145
Keflex	Eli Lilly	Oral antibiotic	1971	$140
Clinoril	Merck	Arthritis	1978	$125

Source: Oppenheimer & Company

APPENDIX "E"

Wall Street report

The Drugs in the Eighties: The Growth Will Be There – Part 1

by James L.L. Tullis

Mr. James Tullis is a principal of Morgan Stanley & Co Incorporated in New York City. He may be reached at (212) 974-4414

Investors desire certainty, to the extent it can be defined. Yet seldom in recent history have the capital markets reflected as high a degree of uncertainty as they do today. For example, currently the cost of debt capital is both very high and subject to extreme short-term volatility. Moreover, whereas market participants increasingly anticipate recession and disinflation in 1981, economic activity and interest rates continue to be far higher than general expectations.

In this environment, an industry which offers relatively high predictability and which is intrinsically capable of adjusting to a broad range of potential economic scenarios will attract investors. This is particularly true if the fundamental outlook for the business is improving.

STRONG RELATIVE PROFIT PROSPECTS, IMPROVING FUNDAMENTALS

The drug industry's earnings outlook is excellent, both near and longer term, particularly in relation to expected trends in domestic corporate profits. In the 1981 to 1986 period, we expect net income of both ethical and consumer-sensitive pharmaceutical firms to expand more rapidly than in 1975 to 1980. (However, the pickup will be more pronounced in the ethical segment, which is more sensitive to trends in the prescription drug business.)

Specifically, we estimate profits in the ethical drug sector will rise about 12 percent in 1981, while earnings in the consumer-sensitive category expand 5 percent if Warner-Lambert with its large write-offs is included or 10 to 11 percent excluding Warner-Lambert. By contrast, corporate profits are now forecast to rise 3 to 4 percent this year. On an operating basis, the industry's performance should be even more impressive than these earnings projections indicate, because our estimates include the impact of the severe currency-related penalties which all of the heavily multinational drug firms are incurring this year as a result of the dollar's continuing strength. (We think currency factors will reduce drug profits overall by 5 to 10 percent this year.)

In 1982, industry earnings growth should be especially strong. Our preliminary forecasts, as detailed in **Table 1**, call for profit gains of close to 20 percent in both the ethical and consumer-sensitive segments next year. Such increases would outpace the 10 percent advance forecast for profits in general, even in the rapid recovery stage of an economic expansion.

In 1983 to 1986, we anticipate earnings growth in the ethical drug sector will average about 15 to 16 percent per year, which represents a significant premium above the 7 to 8 percent gains projected for corporate profits.

Consumer-sensitive firms should also post net income advances exceeding those of the S&P 400 in that interval, although the expected earnings expansion (12 to 14 percent per annum) will be less rapid than that in the ethical category.

Based on these projections, drug stocks should retain considerable appeal well into the next economic expansion. In addition, the group's investment attractiveness should be enhanced by a number of other factors:

- The liquidity of the pharmaceutical industry remains very high, with almost all firms retaining substantial cash positions which exceed short-term debt and in most cases total borrowings. As a result, three benefits accrue: **(1)** high short-term interest rates generally help earnings, as interest income more than offsets interest expenses; **(2)** dividends can be increased faster than profits expand (as was the case in 1979 and 1980); and **(3)** companies have funds to repurchase stock in the open market, aiding per share earnings comparisons (more than half of the drug firms currently have active stock repurchase programs).
- The drug industry, which has demonstrated its general ability to cope with inflation by raising prices and controlling costs, should also be a significant beneficiary of disinflation. Pharmaceutical firms would begin to feel the impact of diminishing cost increments before the rate of price hikes slowed; thus, margins would improve early on. Importantly, our five-year earnings forecasts for the

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Table 1. Healthcare Industry: Current Earnings Estimates

Industry Segment	Price 5/26	Div. Rate Per Share		Yield		Earnings Per Share				P/E Ratio			EPS Next Quarter		
		Cur.	12/81	Cur.	12/81	1979A	1980	1981E	1982E	1980	1981E	1982E	1980	1981E	Ending
Hospital Supply															
ABT	56.00	1.44	1.44	2.57	2.57	2.97	3.46	4.05	4.75	16.18	13.83	11.79	0.85	1.00	JUN
AHS	46.00	1.08	1.08	2.35	2.35	2.78	3.03	3.55	4.20	15.18	12.96	10.95	0.76	0.81	JUN
BAX	56.00	0.76	0.76	1.36	1.36	3.02	3.40	3.87	4.63	16.47	14.47	12.10	0.87	0.94	JUN
BDX	47.00	1.00	1.17	2.13	2.49	3.01	3.14	3.55	4.00	14.97	13.24	11.75	0.80	0.88	JUN
MDT	40.00	0.48	0.60	1.20	1.50	2.52	2.80	3.50	4.25	14.29	11.43	9.41	0.80	0.80	APR
Consumer Sensitive															
AHP	34.00	1.80	2.02	5.29	5.94	2.51	2.84	3.20	3.63	11.97	10.63	9.37	0.64	0.71	JUN
BMY	53.00	1.84	1.84	3.47	3.47	3.50	4.08	4.55	5.15	12.99	11.65	10.29	0.97	1.06	JUN
JNJ	106.00	2.30	2.60	2.17	2.45	5.76	6.50	7.35	8.70	16.31	14.42	12.18	1.63	1.86	JUN
MNP	31.00	1.52	1.65	4.90	5.32	3.40	3.52	3.70	4.11	8.81	8.38	7.54	0.56	0.70	JUN
STY	22.00	0.92	1.03	4.18	4.68	1.85	2.04	2.20	2.45	10.78	10.00	8.98	0.42	0.43	JUN
WLA	23.00	1.32	1.35	5.74	5.87	1.55	2.41	0.52	2.50	9.54	44.23	9.20	0.69	0.58	JUN
Ethical Drugs															
LLY	62.00	2.30	2.70	3.71	4.35	4.43	4.52	5.17	6.35	13.72	11.99	9.76	0.98	1.03	JUN
MRK	91.00	2.60	3.00	2.86	3.30	5.06	5.54	6.20	7.40	16.43	14.68	12.30	1.47	1.57	JUN
PFE	48.00	1.60	1.65	3.33	3.44	3.26	3.48	3.70	4.60	13.79	12.97	10.43	0.79	0.79	JUN
SGP	37.00	1.60	1.73	4.32	4.68	4.12	4.45	4.60	5.25	8.31	8.04	7.05	1.20	1.22	JUN
SRL	31.00	0.52	0.52	1.68	1.68	1.68	1.85	2.25	2.65	16.76	13.78	11.70	0.46	0.49	JUN
SKL	83.00	1.92	2.30	2.31	2.77	3.78	4.65	5.70	6.75	17.85	14.56	12.30	1.04	1.27	JUN
SQB	36.00	1.20	1.25	3.33	3.47	2.71	2.65	2.70	2.95	13.58	13.33	12.20	0.50	0.47	JUN
SYN	58.00	1.30	1.60	2.24	2.76	3.77	4.28	5.45	6.35	13.55	10.64	9.13	1.03	1.35	APR
UPJ	63.00	2.00	2.25	3.17	3.57	5.03	5.71	6.25	7.07	11.03	10.08	8.91	1.53	1.60	JUN

E = Morgan Stanley Research Estimate

industry would not be significantly changed if the underlying inflation rate dropped to 6 percent from the 8 to 9 percent level forecast.

- Political and governmental trends, still an important element in the industry's outlook, have become more favorable. Under Reagan Administration directives to reduce Federal red tape, the pace of new-drug approvals should accelerate. Also, the probable attempt to cut down the extremely large existing backlog of pending new-chemical entity applications (as shown in Table 2) could result in a significant short-term spurt in the number of products coming to market. In addition, chances have increased that Congress will eventually pass legislation to extend the duration of patent protection for pharmaceuticals, providing long-needed relief for the industry.
- There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced.
- Although drug stocks have performed well for the past three years, the shares of almost all pharmaceutical companies are inexpensive by historical standards (Figure 1). Since 1946, the multiple premium accorded to the drug companies relative to the S&P 400 averaged about 70 percent, in a range of 20 to 150 percent (excluding one brief period in the early 1950s when the group commanded no premium and two longer intervals in the late 1940s and early 1970s when the stocks sold at price/earnings ratios more than 200 percent above that of the composite). Currently, drug shares are valued about 33 percent and 24 percent above the multiples of the S&P 400 based on estimated 1981 and 1982 earnings, respectively. At the same time, the ratio of the industry's profit growth rate to that of the composite is near peak levels.

WHY ARE DRUG FIRMS DOING WELL?

The current strong and improving fundamental position of the drug industry is best appreciated in the context of past experience. Between 1945 and 1974, pharmaceutical company sales and profits grew, on average, at an annual rate of 10 percent. Earnings gains followed a relatively predictable cycle, expanding as much as 20 percent a year during economic advances and only about 2 percent during economic contractions. From 1975 to 1977, the industry went through a sustained three-year period of laggard (less than 10 percent per annum) profit expansion at a time when many other sectors were

Table 2. New Chemical Entity NDAs Awaiting FDA Approval in the United States

Industry Segment	Estimated New Chemical Entity NDAS Currently Before FDA	R&D Spending 1979	R&D Spending 1980	R&D Spending 1981E
			($ Millions)	
Consumer Sensitive				
American Home Products	4	$ 90.0	$102.0	$116
Bristol Myers	4	103.0	128.0	150-155
Johnson & Johnson	3	192.7	232.8	280
Morton Norwich*	2	19.2	21.8	24
Sterling	0	48.9	58.1	68
Warner-Lambert	1	94.0	103.0	116
Ethical Drugs				
Eli Lilly	3	177.0	200.7	230-235
Merck	5	188.1	233.9	280.0
Pfizer	5	138.0	160.0	190.0
Schering-Plough	4	75.0	90.0	110.0
Searle	2	59.5	71.3	90.0
SmithKline	0	103.0	136.0	170.0
Squibb (*Capoten* just approved)	0	69.0	77.0	90.0
Syntex*	1	42.0	54.0	66.0
Upjohn	6	129.3	147.3	160.0

*Fiscal 1979, 1980, and 1981, respectively

Morgan Stanley Research Estimates

registering extremely robust increases. There were several reasons for the relatively disappointing performance of drug firms:

(1) Inflation had accelerated, but pharmaceuticals manufacturers, following a 30-year record of stable pricing policies overall, were loath to increase prices aggressively. At the time, Senator EDWARD KENNEDY was holding regular hearings on industry practices before a liberal, Democratic Congress, presumably hostile to drug company profits.

(2) Unit volume growth was poor (3 to 4 percent a year domestically versus a historical trend of 7 to 8 percent), as only a handful of new products was introduced and as side-effect concerns pared consumption of certain leading products (such as oral contraceptives, tranquilizers, antibiotics, and some analgesics like *Darvon*).

(3) An initial attack on drug prices by many foreign governments hurt foreign earnings just as the sustained three-year strengthening of the United States dollar caused large penalties on the translation of overseas profits into dollars. Drug industry net income still expanded from 1975 to 1977 – but at less compelling rates than in many prior years and less rapidly overall than earnings of the S&P 400.

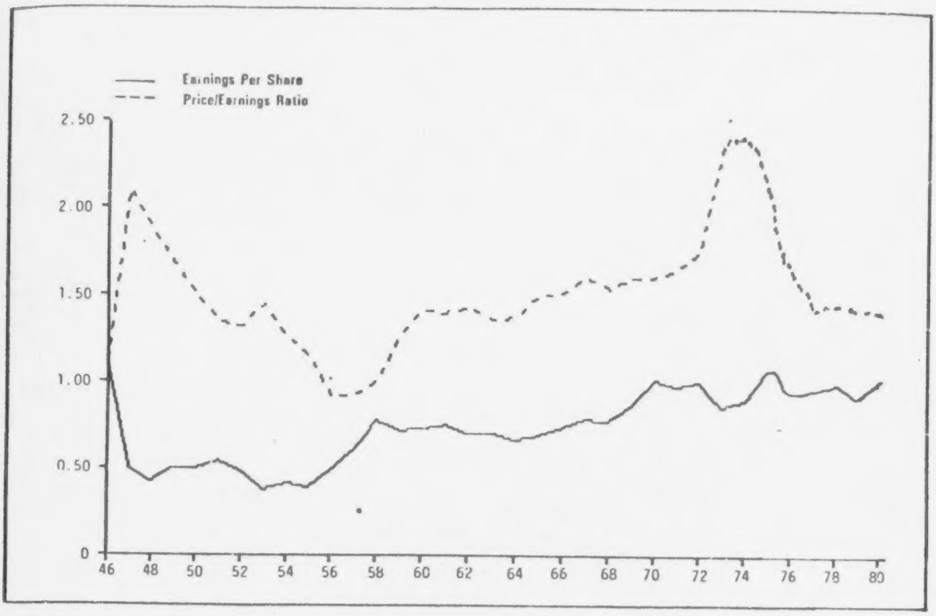
From 1978 to 1980, the industry's vitality improved for several reasons. Drug firms gradually became more willing to increase prices. By 1980, the annual rise in realizations reached 8 to 9 percent, a level since surpassed. Domestically, governmental agencies, which pay for only a very small portion of all drug purchases, and consumers showed no sign of resistance. Senator Kennedy's hearings ended quietly. Unit volume gains were helped (a bit) by new-product introductions. Also, the dollar weakened, and currency impacts became positive rather than negative. Foreign governments learned that drugs represent but a small portion of healthcare costs and are economically efficient; thus, officials gradually began to allow price increases. Tight cost controls put into effect in 1976 and 1977 started to exert a favorable impact on margins. Profit momentum improved, with the industry registering double-digit gains of 19 percent, 15 percent, and 11 percent in 1978, 1979, and 1980, respectively. Table 3 shows trends in pretax profits in the 1975 to 1980 period and our estimates for 1981 and 1982.

The gains forecast for this year and next are surprisingly strong, especially when one considers that currency trends will probably have a more adverse impact on profits in 1981 than in any prior year while the economic outlook has weakened, with at least a mild recession now expected in the second half of the current year. In the following sections, we will discuss the assumptions used in developing our earnings model.

DOMESTIC MARKET OUTLOOK 1981–1982

We project that overall prescription dollar volume in the domestic market will expand rapidly (up 15 to 17 percent) in 1981 and as fast (or perhaps a bit faster) in 1982.

Figure 1. Standard & Poor's Drug Index Relative to 400 Industrials



Source: Morgan Stanley Research

The potential for further acceleration in 1982 derives from the possibility that the Food and Drug Administration (FDA) will "unjam" the large backlog of new drugs awaiting domestic marketing approval. The primary element in the strong sales growth forecast for 1981 and 1982 (compared with historical 10 percent per annum trendline increases) is higher drug prices. We estimate realizations will rise at a double-digit (10 to 12 percent) rate in 1981 – faster than in any prior year – and 9 to 10 percent in 1982. Our projections for next year assume a slightly slower pace of price boosts, as the Morgan Stanley economic forecast indicates inflation should moderate by then. However, if inflation remains high, we think the rate of drug price expansion will also stay high.

It is important that investors recognize that drug unit demand is not sensitive to price. In many businesses (e.g., autos, soft drinks, and restaurants), the price increases needed to maintain margins during a period of high inflation eventually lead to reduced consumption. However, demand for prescription drugs is uniquely price insensitive because (1) the cost/benefit equation is extremely favorable; (2) the patient has less to do with the purchase decision than his doctor, who is not paying the bill; and (3) the average patient spends only about $40 to $45 per year on prescription drugs – a remarkably small absolute amount. Reflecting these elements, surveys show that consumers have remarkably little awareness of or concern about drug prices. Also, Federal and state government purchases represent a very small (10 percent at most) portion of drug volume, and government (in this country) has no real control over drug pricing.

We forecast unit volume will increase 4 to 5 percent this year, a slightly higher gain than in the past five or six years, but still below the long-term trend. In 1982, we expect unit volume expansion to accelerate to 6 to 7 percent, primarily because of better economic conditions but also because of an increased flow of new products to market. If the FDA can straighten out its approval processes and actually begin to catch up on long overdue approvals, unit volume growth next year might exceed 7 percent. It seems clear that the number of new-drug approvals granted in 1982 will be higher than the 12 of

Table 3. Healthcare Industry: Pretax Earnings (1975-1982)

($ Millions)

Health Industry Segment	Amount								Year-to-Year % Change						
	1975	1976	1977	1978	1979	1980[a]	1981E	1982E	1976	1977	1978	1979	1980[a]	1981E	1982E
Hospital Supply															
Abbott	102.40	138.00	183.40	233.70	282.60	337.66	391.11	451.27	34.77	32.90	27.43	20.92	19.48	15.83	15.38
Amer. Hosp. Supply	97.70	117.70	134.40	147.90	155.00	187.00	222.00	266.00	20.47	14.19	10.04	4.80	20.65	18.72	19.82
Baxter Travenol	55.60	84.50	108.10	119.10	145.00	164.00	192.00	231.00	51.98	27.93	10.18	21.75	13.10	17.07	20.31
Becton, Dickinson*	62.20	75.90	84.40	93.20	102.00	100.00*	110.00	126.00	22.03	11.20	10.43	9.44	−1.96[b]	10.00	14.55
Medtronic**	25.10	23.60	27.80	39.90	53.17	64.80	80.91	102.00	−5.98	17.80	43.53	33.26	21.87	24.86	26.07
Total	343.00	439.70	538.10	633.80	737.77	853.46	966.02	1176.27	28.19	22.38	17.78	16.40	15.68	16.70	18.10
Consumer Sensitive															
Amer. Home Prds.	496.50	544.40	596.40	682.30	751.00	852.00	960.00	1075.00	9.65	9.55	14.40	10.07	13.45	12.68	11.98
Bristol-Myers	257.80	288.70	329.00	375.70	421.00	490.00	546.00	615.00	11.99	13.96	14.19	12.06	16.39	11.43	12.64
Johnson & Johnson	318.80	361.50	432.20	514.20	590.00	675.00	774.00	912.00	13.39	19.56	18.97	14.74	14.41	14.67	17.83
Morton-Norwich***	33.90	7.50	54.60	62.10	76.80	72.96	77.87	87.29	−77.88	628.00	13.74	23.67	−5.00[b]	6.73	12.10
Sterling	145.80	153.50	163.40	183.80	200.00	222.00	235.00	262.00	5.28	6.45	12.48	8.81	11.00	5.86	11.49
Warner-Lambert	289.00	296.00	341.00	362.00	231.00	330.00	125.00	364.00	2.42	15.20	6.16	−36.19	42.86	−62.12	191.20
Total	1541.80	1651.60	1916.60	2180.10	2269.80	2641.96	2717.87	3315.29	7.12	16.05	13.75	4.11	16.40	2.87[c]	21.98[c]
Ethical Drugs															
Eli Lilly	301.50	346.10	394.50	482.50	558.00	590.00	670.00	808.00	14.79	13.98	22.31	15.65	5.73[b]	13.56	20.60
Merck	378.30	416.40	453.50	507.90	606.00	655.00	717.00	853.00	10.07	8.91	12.00	19.31	8.09[b]	9.47	18.97
Pfizer	211.90	237.90	263.60	319.30	363.00	409.00	448.00	557.00	12.27	10.80	21.13	13.69	12.67	9.54	24.33
Schering-Plough	210.50	234.40	241.60	272.70	307.00	326.00	338.00	388.00	11.35	3.07	12.87	12.58	6.19[b]	3.68	14.79
Searle	93.50	89.60	106.10	121.60	134.00	138.00	167.00	202.00	−4.17	18.42	14.61	10.20	2.99	21.01	20.96
SmithKline	94.20	107.10	134.30	261.30	354.00	446.00	546.00	652.00	13.69	25.40	94.56	35.48	25.99	22.42	19.41
Squibb	134.90	147.40	154.70	150.50	149.00	159.00	171.00	196.00	9.27	4.95	−2.71	−1.00	6.71	7.55	14.62
Syntex	48.90	49.30	46.50	62.90	75.00	89.00	116.00	138.00	0.82	−5.68	35.27	19.24	18.67	30.34	18.97
Upjohn	120.20	128.30	147.60	202.00	204.00	230.00	249.00	291.00	6.74	15.04	36.86	0.99	12.75	8.26	16.87
Total	1593.90	1756.50	1942.40	2380.70	2750.00	3042.00	3422.00	4065.00	10.20	10.58	22.56	15.51	10.62	12.49	19.37
Health Industry Total	3478.70	3847.80	4397.10	5194.60	5757.57	6537.42	7135.89	8576.56	10.61	14.28	18.14	10.84	13.54	9.15	20.19

*Fiscal years ended September 30

**Fiscal years ended April 30

***Fiscal years ended June 30

[a] Results shown are after the effect of change to LIFO accounting by five firms in 1980. Before the effect of these accounting changes, pretax profits and rates of increase of these segments and total industry were: Hospital Supply, $867.76 million, up 17.62%, Consumer Sensitive, $2,653.66 million, up 16.91%, Ethical Drug, $3,126.80 million, up 13.7%, and Industry Total $6,648.22 million, up 15.47%.

[b] After the effect of switching to LIFO Accounting, which reduced reported 1980 results. Had FIFO accounting been used in both years, pretax earnings growth rates would have been, respectively: 10.23% (Morton-Norwich), 12.06% (Becton, Dickinson), 11.68% (Eli Lilly), 13.76% (Merck), and 11.79% (Schering-Plough).

[c] Warner-Lambert is accruing $134.3 million of one-time charges in 1981. Excluding the effect of these write-offs, the Consumer Sensitive segment's rate of increase in pretax earnings would be 13.59% and 16.84% in 1981 and 1982, respectively.

E = Morgan Stanley Research Estimates

1980. Most observers consider 15 to 20 per year a realistic target, in view of history and the current backlog on file.

Both new FDA Commissioner HAYES and Secretary of Health and Human Services SCHWEIKER are on record supporting a much faster pace of drug approvals. Congressmen GORE and SCHEUER, noted liberal Democrats, recently sponsored legislation aimed at accelerating the pace of new-drug clearances. Congress is now holding hearings on the proposals (we recently attended one and were impressed by how rapidly the message of the 1980 elections has sunk in). We anticipate that the legislators will actually help, not hinder, SCHWEIKER and HAYES in spurring the FDA bureaucracy into action.

Also, there is a remarkably large backlog of drugs now awaiting approval. As **Table 2** shows, the leading United States drug firms now have some 40 completed new-drug applications (NDAs) for completely new chemical entities on file pending Government action (plus many more NDA submissions for combination products, new dosage forms, or additional claims). Foreign drug manufacturers who sell here probably have another 20 to 30, at least. We think it is possible that to clear up this backlog, the FDA will speed up the review of completed NDA submissions. If this occurs, it is conceivable that the number of approvals could spurt to 25 or more in 1982 and 1983, which would stimulate unit volume growth in the United States market.

Table 4. New Chemical Entity NDAs with Very Large Commercial Potential Now Awaiting United States Approval

Company	Drug	Field of Therapy	Why Unique	Estimated U.S. Sales ($ Millions) 1982	Estimated U.S. Sales ($ Millions) 1985
Johnson & Johnson	*Ketoconazole*	Fungal Disease	Superior efficacy	$60	$150
Lilly	*Opren*	Arthritis	Once-a-day dosage No G-I side effects May induce remission	50	150
Lilly	*Moxalactam*	Antibiotics	Superior efficacy	60	150
Marion	*Cardiem*	Cardiovascular	Superior efficacy	15	100
Merck	*Blocadren*	Cardiovascular	Same as other beta blockers, but may also be labeled as protective against heart attacks	30	125
Merck	*Moduretic*	Cardiovascular	Comparable efficacy but less toxicity	30	100
Merck	*Ivermectin*	Anthelmintic (animal use only)	Superior efficacy	40	100
Pfizer	*Procardia*	Cardiovascular	Superior efficacy	40	125
Pfizer	*Feldene*	Arthritis	Once-a-day dosage	90	150
Pfizer	*Cefobid*	Antibiotic	Superior efficacy	30	100
Searle	*Verapamil*	Cardiovascular	Superior efficacy	45	125
Upjohn	*Xanax*	Psychopharmaceutical	Possible dual claim for anxiety and depression	25	100

Morgan Stanley Research Estimates

Assessing the NDAs now on file, certain drugs have especially promising prospects. In our opinion, the applications for products with the greatest relative commercial potential and impact on earnings are those of Johnson & Johnson, Eli Lilly, Merck, Pfizer, and Searle. This evaluation is an important factor in our purchase recommendations on the last four issues. As highlighted in **Table 4**, the specific drugs with the most exciting commercial prospects are Pfizer's *Procardia, Feldene,* and *Cefobid,* which together could generate more than $100 million in incremental sales for the company domestically next year (and more overseas); Merck's *Blocadren, Moduretic, Ivermectin,* and *Tocainide,* which have ,a similar or greater composite potential; Lilly's *Opren* and *Moxalactam,* which are expected to add at least $100 million in sales in the United States (and more overseas); Johnson & Johnson's *Ketoconazole,* a breakthrough improvement in fungal disease treatment with long-term commercial potential in the $100 million or greater range; and Searle's *Verapamil,* which we forecast will be the most heavily used calcium antagonist by 1984 or 1985. The calcium antagonists are the next major wave of cardiovascular treatment agents and, in our opinion, will represent a domestic market of $250 million or more (and worldwide volume of $1 billion) by 1985.

We also expect the domestic volume gains forecast for 1981 and 1982 to be accompanied by margin expansion. Profitability of drug sales in the United States is improving currently (and should continue to do so for the next several quarters) because higher prices are more than offsetting inflationary cost pressures. The gross margin is gradually increasing, and SG&A costs should only rise about 11 to 12 percent this year and next (i.e., less rapidly than revenues). In summary, we forecast domestic pretax profits will grow about 20 percent in 1981 and 21 to 25 percent in 1982. Since the composite (i.e., domestic plus foreign) profit gains projected for the industry are considerably lower (12 percent) in 1981 and somewhat smaller (19 percent) in 1982, it is clear that we anticipate international earnings will expand much more slowly than those from domestic sources and also less rapidly than the historical 15 percent per annum trend.

Part 2 of this report will appear in the September MM&M. Included will be discussion of the years 1981 to 1982 – the international market outlook, who will register the strongest gains, which firms could provide profit surprises – along with analysis of the longer-term outlook.

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Mr. ENGELBERG. I am Alfred Engelberg, patent counsel to the Generic Pharmaceutical Industry Association and a partner in the firm of Amster, Rothstein & Engelberg of New York City. I have been engaged in the practice of patent law for over 20 years and during that time had positions in the Government, in industry, and in private practice.

The term "effective patent life" is the creation of those who are promoting patent extension legislation and has no counterpart in patent law or the fundamental philsophy on which the patent system is based. Indeed, the notion that the 17-year patent grant carries with it any guaranty that the patent owner will enjoy 17 years of commercial exploitation of the patented invention is contrary to that philosophy as well as the requirements which must be met to obtain a patent.

From a philosphical standpoint, the patent system was established to promote the progress of science and the useful arts by encouraging early disclosure of ideas and inventions in the belief that such disclosures would prevent wasteful duplication of research and would stimulate further inventions and improvements which in the long run would obsolete the earlier disclosed inventions. Reward to the inventors was secondary.

The system was clearly designed to benefit society and although some reward was deemed essential, the reward is not in the form of a positive grant of a fixed period of monopoly. Indeed, anyone who takes a look at the patent law will find that the right granted in a patent is the right to exclude others for 17 years from making, using or selling the invention, and not a positive right to commercial exploitation.

Until this controversy, no one connected with the patent system believed that any fixed period of commercial exploitation existed. In fact, it is contrary to most of the rules that we deal with in the sense that prior public use, commercialization, or even publication of an invention before a patent application is filed is a bar to an invention in this country after 1 year and immediately throughout the rest of the industrialized world. In fact, I would note for Mr. Walker's benefit—if he were here—that there is no patent on Rubik's cube because Professor Rubik published a paper on that cube before he realized its commercial implications.

That points to a very important point in connection with this proceeding, and that is that the patent grant is a reward for disclosure of the invention. It is not a reward for investment or for commercial exploitation. That patents were never intended to define a fixed period of commercial exploitation is reinforced by a variety of patent rules and practices.

For example, the patent law contains no requirement that a patentable idea be at any particular stage of development before a patent application can be filed. It is perfectly permissible to file a patent application on a concept which has never been tested and which is far broader than a limited concept which has actually been tested.

Mr. Hutt indicated in his remarks that a specific utility and process must be set forth in a patent application. That is true in only the broadest sense. It is all an allegation of a utility and some form, not necessarily a commercial form, for manufacturing a product that must be set forth in a patent.

In pharmaceutical composition cases, it is common to define invention by a broad hypothetical formula that encompasses hundreds or thousands of compounds with only a few limited examples that have actually been tested. Unfortunately, most laymen believe that when a patent issues, it covers only the commercial device that is actually going to be made under the patent and, in fact, the whole extension controversy and the way the bill is structured is based on that premise when, in fact, it is not the case.

Another variable which clearly indicates that there is no notion of an exploitation right in the patent law is that a patent application can be filed anytime the inventor chooses to file it. It can be filed when the idea first arises. It can be filed when the product is 90 percent of the way toward commercial development, or anyplace in between, and the choice is strictly up to the inventor provided he maintains secrecy.

The reason most patent applications are filed early in the game is a fear that someone else will make the invention first, but that is part of the competitive system and part of the fundamental idea that the patent system is designed to encourage.

Another point which has been alluded to several times during the proceedings here today is that the 17-year patent monopoly runs only from the date that the patent is granted. That is true, but it is also true that the inventor has a great deal of control over what the period of patent pendency turns out to be.

In many situations, a broad speculative patent application is filed in the first instance, and it is followed later on by a series of further patent applications which home in on an invention as the research backing up the patent disclosure develops.

Another rule that was skimmed over, I think, somewhat by Mr. Hutt is that by law a patent must be limited to a single invention, and in many instances the method of making a product or the method of using a product are required to be set forth in separate patent applications from the application which covers the product itself.

What this means is that although a document you look at may well describe a use, a method, and a product, the claims of that patent, which are really the only important part of the monopoly which one gets, may be limited strictly to the product. The Patent Office may well require you to file a separate application to cover the process and yet a separate application to cover the method of use, and those patent applications will follow different tracks in the Patent Office, are subject to different rules as the timing of filing, and will issue at different dates.

So there is no guarantee that because you see a patent and it has expired, that you can even practice the process or the method of use that is described in that patent document. I will give you a couple of specific examples later on in this presentation.

Those are only some of the rules. Those of us who are skilled in the practice of patent law have learned to manipulate those principles in order to have dramatic impact for our clients on both the scope and length of the commercial monopoly.

Obviously, there are many tradeoffs in the process. For example, if you file a very broad patent application very early in a research project, obviously the date of initial commercial exploitation is going to be many years later than it would be if you filed it later on in the process. That is going to have an effect on what we have been calling effective patent life.

Indeed, because of the way patent applications are filed—and I think this is tremendously important in view of some of the remarks here today—it may well be that the actual compound which is ultimately commercially marketed is not even described in the patent although it is covered by the patent.

How does that happen? It happens because patent claims are directed to broad hypothetical formulas covering these hundreds or thousands of compounds which I mentioned. The specific commercial form of the product may not be discovered until even after the patent issues. That leads to a very interesting point because if you subtract 8.3 years from 17 years, which is the alleged development time, you end up with an effective patent life of less than 9 years.

But the reason for that lowering of the effective patent life is the invention was not made at the time the patent issued. The broad concept of the invention may have been known, but the specific composition was not known.

My paper cites an article by Rudolph Anderson, a leading advocate for patent extension. He states in his own article that the discovery of the commercial form of the compound after the patent issues is a common occurrence.

So I suggest to the committee that when the data is analyzed, as to effective patent life, one take a look not only at the delay in filing IND's but also determine whether or not the compound for which an NDA is being sought is actually described in the patent document for which an extension is sought.

This makes a tremendous difference in what we are talking about, and is a problem that is not caused by regulatory delay but a problem caused by the fact that people want to file patent applications early in order to block out broad fields of preserved research for themselves.

The fact of the matter is that patent applications are published abroad within 18 months of the time they are filed here. The industry looks at them. The industry sees there is no point in going into that field of chemistry. Company X has that tied up. That gives Company X free rein in the ensuing years to refile, to file multiple generations of patent applications, to modify formulations, and to be in control of an area of technology for a very, very long time.

Mr. GORE. Mr. Engelberg, that is an excellent point, and I would hate to miss any other points of similar value; if you could preserve the value of your statement and yet summarize the remaining portion, it would be appreciated.

Mr. ENGELBERG. I want to give two quick examples, and then I think I can wrap up, to show how the rules affect patent life and to relate it back to something said this morning.

The patent application on Valium was filed in 1959 and it covered not only Valium but one of these hypothetical formulas involving a host of compounds that had not been produced or tested. By 1960 the patent examiner advised Roche that they were willing to grant a patent which specifically covered Valium, but not the broad coverage because of a lack of specific disclosure to support them.

Roche did not accept the broad patent. The procedures relating to these matters consumed approximately 8 years, and no patent covering Valium was issued in the United States until 1978. By using this technique Roche was able to get 22 years of effective patent life.

As I understand, the NDA approval was actually obtained in 1963, and I would like to note here that I think it is highly relevant to the question of whether or not the further additional data is necessary—the one point that I do not think has been clearly made in the proceedings this morning is that if the regulatory period or a substantial portion of the regulatory period can occur while the patent is pending, there is no effective reduction of patent life, and a decision as to when to start the IND process is in the hands of the patentee. If he starts early, he preserves effective patent life. If he starts late, he chops away at effective patent life. The Congress is being asked to give back time to the drug industry that they themselves have elected to lose, and I think that is why the data is relevant.

To briefly turn to the Keflex example cited in my statement, Keflex represents a situation in which there are actually two patents covering the same product, one broad, one narrow, each having different effective patent lives, and demonstrates a situation where the expiration of the first patent does not leave you free to manufacture the commercial compound.

My statement includes many of the same comments on the 1980 PMA study that were noted this morning, but there is one other point I think that should be made here, There is clearly a potential adverse effect for patent extension on innovation, given the complex world of patent claims, because the proposed legislation would extend the enforcement of those claims without regard to the circumstances giving rise to the extension. It is entirely possible in the innovative world that we live in that a third party independent of the patentee will discover a new use for a patented compound.

Under the bill as written, the patentee could file an NDA, do some clinical research, and get an extension on his patent which would apply not only to the new use but to all the old uses. This makes no sense. It undermines the patent system, since the purpose of having those disclosures in patents is to spur further innovation.

Thank you.

[The prepared statement of Alfred B. Engelberg follows:]

STATEMENT OF

ALFRED B. ENGELBERG

PATENT COUNSEL

GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION

BEFORE THE

COMMITTEE ON SCIENCE AND TECHNOLOGY

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

UNITED STATES HOUSE OF REPRESENTATIVES

ON

PATENT TERM EXTENSION AND PHARMACEUTICAL INNOVATION

FEBRUARY 4, 1982

My name is Alfred Engelberg, and I am Patent Counsel to the Generic Pharmaceutical Industry Association and a partner in the firm of Amster, Rothstein & Engelberg of New York City. I have been engaged in the practice of patent law for over twenty years and during that time period, have been a Patent Examiner in the United States Patent and Trademark Office, a patent attorney for a large multi-national corporation, a patent trial attorney for the United States Department of Justice, and a private practitioner.

This Committee and other Congressional Committees have been attempting to define the factors which influence "effective patent life" and have heard much debate as to how it should be measured and whether it is rising or falling. A fundamental reason for the difficulty in defining these factors is that the term "effective patent life" is the creation of those who are promoting patent extension legislation and has no counterpart in patent law or the fundamental philosophy on which the patent system is based. Indeed, the notion that the seventeen year patent grant carries with it any guaranty that the patent owner will enjoy seventeen years of commercial exploitation of the patented invention is contrary to that philosophy as well as the requirements which must be met to obtain a patent.

From a patent philosophy standpoint, the decisions of the United States Supreme Court over more than a century clearly point out that the patent system was established to promote the progress of science and the useful arts by encouraging inventors to make early disclosure of their inventions to the public in the belief that such disclosures would prevent wasteful duplication of research and would stimulate further inventions and improvements which, obviously, would render the earlier disclosed inventions obsolete. The system was clearly designed to benefit society and not to reward inventors, although it has always been recognized that some reward is essential as an inducement for the invention disclosure. The inducement provided by the patent law is not a positive grant of the right to commercial exploitation of the invention but, rather, a negative grant, namely, the right to exclude others from making, using or selling the invention for a period of seventeen years.

Until the present controversy concerning patent extension, no one connected with the patent system believed or argued that the grant of a patent created a positive right to exploitation for a fixed period of time. Indeed, that notion conflicts with one of the basic requirements to the issuance of a valid patent, namely, that the subject matter of the patent cannot have been used or sold commercially for more than one year prior to the date on which a patent application is filed. This rule exists because the patent grant is a reward solely for disclosure of the invention and not a reward for either its discovery or for an investment in its commercial development and exploitation. The patent extension concept is a radical departure from that philosophy.

That patents were never intended to define a fixed period of commerical exploitation is reinforced by a variety of fundamental patent rules and practices which give inventors enormous control over both the scope and issue date of a patent. These include the following:

a. The patent law contains no requirement that a patentable idea be at any particular stage of development before a patent application can be filed. In fact, it is perfectly permissible to file a patent application on a concept which has never been tested or which is far broader than the limited concept which has actually been tested. In pharmaceutical composition cases, for example, it is quite common to define the invention by a broad hypothetical formula which encompasses hundreds or thousands of possible compounds having certain structural similarities, even though, at the time the original patent application is filed, only a small handful of compounds have actually been made and tested. Unfortunately, most laymen believe that patents are much more limited in scope and cover only the very specific and well developed products or processes which are actually commercially exploited.

b. Assuming that there has been no commercial exploitation of an invention, an inventor is free to file a patent application at any time in the development of a new idea. Obviously, if no patent application is filed until the invention is reasonably well along in the development process, it is likely that the inventor will enjoy a longer period of commercial exploitation. By waiting, the inventor runs some risk that others will file patent applications on the same invention, but the patent law protects the first actual inventor and not the first person to file a patent application, provided that adequate records are kept to establish the conception and development of the invention.

c. The seventeen year patent monopoly runs from the date on which the patent is actually granted after it is examined by the United States Patent and Trademark Office and does not run from the filing date of the patent application. How long a patent application remains pending in the Patent Office is highly variable and, to a significant extent, can be controlled by the inventor. It is entirely permissible to keep a patent application pending for a long time by abandoning the original patent application in favor of so-called continuation or continuation-in-part applications which supplement or expand upon the original invention disclosure based on work carried out by the inventor subsequent to the original application filing date. The use of this practice is widespread and has been a common practice in the pharmaceutical industry.

d. By law, a patent must be limited to a single invention and, in many instances, the method of making a product or the method of using a product are required to be set forth in separate patent applications from the application which covers the product itself. This practice leads to a multiplicity of patent applications, all of which travel through separate tracks in the Patent Office and may issue at separate times. Accordingly, it is entirely possible for a patent covering a product to issue on one date, while a patent covering a use for that product issues on a separate and later date. Accordingly, the expiration of a single patent cannot be automatically equated with a loss of commercial monopoly because there may be other patents which dominate the making or using of that product.

The foregoing are only some of the major rules of the game. Patent attorneys experienced in the manipulation of these principles have the ability to make tactical decisions which can have a dramatic effect on the scope or length of a commercial monopoly, and there are many potential trade-offs in the process. For example, the early filing of an extremely broad patent application covering a broad class of chemical compounds based on preliminary research with only a handful of compounds makes it more likely that the date of initial commercial exploitation of a product may not occur until long after the patent issues. Indeed, the actual compound to be marketed may not even be known at the time the patent application is filed or the patent issues, even though the patent contains broad claims which cover it. In an article entitled "Patent Term Restoration" (APLA Journal, Vol. 8, No. 4, 1980), Rudolph J. Anderson, Jr., a leading advocate of the patent extension concept, states that this is "a situation of common occurrence." But this apparent loss of effective patent life is entirely voluntary and is not without its benefit. The industry rapidly becomes aware that broad patent protection is being sought by a company in a particular area of chemistry, both as a result of publications in scientific journals and the publication of corresponding foreign patent applications within 18 months of the U.S. filing date. These publications serve to discourage competitive research, thereby preserving that area for one company on a long term basis. Any marginal loss suffered as a result of shortened commercial life for the first broad patent application can, and often is, compensated for by a long and complicated series of additional patent applications covering the methods of use, methods of production, further composition variations, varying dosage forms and the like. It becomes a relatively simple matter in the absence of direct competition to obsolete the original commercial compounds as they near their patent expiration dates and promote the use of a variant covered by a new generation of patents. An alternative strategy, and one which is commonly used, involves the early filing of a broad speculative patent application which is eventually abandoned in favor of one or more continuation or continuation-in-part applications as additional research begins to focus on the preferred compositions. The use of this procedure not only strengthens and broadens the scope of protection, but also postpones the issue date of the patent thereby extending the period of commercial monopoly.

The possible variations are limitless, but two brief examples may serve to illustrate at least some of the foregoing principles. In the case of Valium, the original patent application was filed in December, 1959 and disclosed the specific chemical entity Diazepam which is sold under the Valium trademark. But the patent as filed also contained broad claims to a large class of compounds having a structure similar to Valium, although many of these compounds had never actually been produced or tested. In May, 1960, the Patent Examiner indicated that he was willing to grant a patent which specifically covered Valium, but was unwilling to grant the claims to the broader class of compounds because of a lack of specific disclosure to support them. Rather than accept a patent which covered the specific commercial compound, Roche abandoned the original patent application in favor of a series of continuation-in-part applications which were intended to supplement the original disclosure and support the broader claims. The procedures relating to these matters consumed approximately eight years, and no patent covering Valium issued in the United States until 1968. Roche received NDA approval to market Valium in 1963 and, accordingly, will enjoy twenty-two years of so-called "effective patent life" when the patent expires in 1985. The laws of the United States are far more generous in this regard than the laws in other countries. In most industrialized nations, the patent monopoly expires twenty years after the patent application is filed, so that any procedural delays in obtaining issuance of the patent do not benefit the patentee. Accordingly, the Valium patent expired in much of the rest of the world in 1980.

The history of Keflex, generically known as cephalexin monohydrate, demonstates a different strategy affecting patent life. In that case, the original Lilly patent applications covered only a method of producing a large class of cephalosporin antibiotics. Additional patent applications covering the products of that process were not filed until several years later. At that time, Keflex had still not been discovered. Nevertheless, the product patent application then on file in the Patent Office contained a description of a class of compounds which was so broad that it actually encompassed the undiscovered product. This broad patent issued in 1970, and Lilly received NDA approval to market Keflex in 1971, thereby giving Lilly sixteen years of "effective patent life" despite the fact the product was unknown when the orginal patent application was filed. Obviously, we have come a long way from the disclosure and reward system envisioned by our forefathers. But the story does not end there. Once Lilly actually discovered Keflex, it filed additional patent applications which specifically covered that compound. That patent issued in 1972, and provides Lilly with eighteen years of effective patent life for a narrower claim which specifically covers Keflex. In effect, Lilly has two patents, one broad and one narrow, which cover precisely the same compound. Interestingly, if the Patent Extension Bill passed by the Senate becomes law, Lilly could extend its broad 1971 patent claims covering the undisclosed Keflex for an additional seven years by conducting the experimentation necessary to obtain NDA approval for another member of the broadly claimed class of cephalosporin compounds covered by the same patent claim. This is so because the bill extends the life of the entire patent claim and does not merely provide a limited extension which is commensurate in scope with the work done to obtain a new NDA approval. Twenty three years of commercial exploitation under the protection of a patent monopoly is a fairly hefty reward, particularly when one considers that the specific compound to which that protection extends was not even known or disclosed in the original patent application.

In the face of such examples--and they are not the only examples which could be given--, how do the proponents of patent extension arrive at effective patent life figures of 9.5 years or, more recently, based on new chemical entities approved in 1980, a figure of 7.5 years? Unfortunately, we are not able to fully answer that question, since there is no readily available way to determine either the identity of the patent used to measure effective patent life, or whether it is the only patent which dominates some aspect of the product. A search of Patent Office records for any of the major pharmaceutical companies will reveal that they are the owners of hundreds, if not thousands, of patents, and there is no expeditious way of determining which patents cover any particular product or some important aspect in the production or use of the product without a careful study of each patent by competent patent counsel aided by technical experts. Such studies are extremely time consuming and expensive.

Some interesting questions have arisen, however, as a result of a highly preliminary investigation relating to the PMA chart showing an effective patent life of about seven and one-half years for new chemical entities receiving NDA approval during 1980. For example, the patent corresponding to the Parke-Davis product known as Meclomen is U.S. Patent No. 3,313,848, which issued April 11, 1967. That patent is based on a patent application filed in June 1964 and a series of earlier patent applications dating back to January 1961. The patent application discloses the specific composition of Meclomen, as well as its use an anti-arthritic. What remains a mystery is why no IND application was filed by Parke-Davis until May 1974, some thirteen years after the first patent application covering the compound was filed. This delay is obviously due to factors other than government regulation and could well be due to a lack of commercial interest in the development of the compound at the time of its discovery. Similarly, the patent covering Yutopar (U.S. Patent No. 3,410,944) issued November 12, 1968, on a patent application which was originally filed in the Netherlands in February, 1964. That patent application, which discloses both the specific compound and its end use, was invented by North American Phillips Company of the Netherlands, and not by employees of Duphar Laboratories or Richardson-Merrill. Once again, there is an unexplained delay of at least seven years between the date the compound and its end use were first disclosed in a patent application and the starting date of clinical investigations. The patent covering Ciba-Geigy's Ludiomil raises similar questions. A patent (U.S. Patent No. 3,399,201) was granted on August 27, 1968, based on a series of patent applications which trace back to a patent application filed in Switzerland in November 1960. Here, there is at least a nine year delay between the discovery of the composition and the commencement of clinical investigations. Moreover, this product is not even listed in the 1981 PDR, despite the fact that approval was obtained during 1980. Once again, commercial rather than regulatory questions appear to be at issue. Further, although there is no patent information available, it is apparent that sixteen years elapsed between the issuance of the patent covering Meclan and the filing of an NDA on that compound. Finally, the PMA chart indicates that Burroughs-Wellcome obtained a patent in August 1965, covering the product known as Viroptic. Our search revealed that the only patent issued to Burroughs-Wellcome in 1965 is totally unrelated to that compound.

The foregoing examples serve to demonstrate yet another problem with any attempt to define "effective patent life", namely, that the decision as to how fast to develop a product and when to place that product on the market may be governed by commercial circumstances which are totally unrelated to the patent issue date. When coupled with the fact that patent applications can and are filed on broad concepts, irrespective of their state of development; that the patentee may legitimately control the patent application filing date and patent issue date; and that multiple and overlapping patents covering different aspects of the same product may be obtained, the search for a definition of "effective patent life" or the belief that meaningful statistics may be developed to establish that it is shrinking as a result of government regulation is an exercise in futility. Each product has its own unique development, commercialization and patent history which make such generalizations highly questionable.

What clearly is not questionable is the potential adverse effects of patent extension on innovation given the complex world of patent claims and proposed legislation which would extend the enforcement of those claims without regard to their scope and without regard to the circumstances giving rise to the extension. For example, a December 28, 1981 article in The Wall Street Journal indicates that the discovery that Inderal is useful in limiting the size of a heart attack among high risk patients was developed with government funding. Is Ayerst Laboratories entitled to a seven-year extension of its patent covering Inderal simply because it now files an NDA for that end use? Should that extension, even if granted, give Ayerst up to seven years of additional monopoly protection on the numerous other end uses of Inderal for which it has been sold during its entire patent life? Will companies other than the original patentees invest time and money in developing new uses for previously patented drugs if the discovery of those new uses will lead to extensions of the original patents, thereby blocking them from commercially exploiting the new uses? Will the opportunity for a seven year extension invite the filing of even broader and more speculative patent applications based on even less backup data, so that the practice of actually making the commercial invention long after the patent issues becomes even more commonplace? The proposed legislation does not even recognize that these problems exist, let alone deal with them in any effective manner.

Clearly, to the extent that government regulation causes delay in bringing products to market, that problem should be addressed and solved. The solution to the problem does not, however, reside in tampering with the patent system in a manner which will create broad new monopoly rights that extend well beyond any real or imagined problem caused by pre-marketing regulation of drug products.

Mr. GORE. Thank you very much.

Mr. Haddad, if you could summarize.

Mr. HADDAD. I am William Haddad, president of the Generic Pharmaceutical Industry Association. As you may know, I have been involved with this subject since my association with the late Senator Kefauver from your State.

I would like to clarify two important points. Mr. Clement, Congressman Walker and I had a brief discussion earlier this morning. He shared a misconception that this legislation only impacts the IND and NDA period. That is inaccurate. As drafted, it predates the IND period.

Mr. CLEMENT. That is clearly incorrect.

Mr. HADDAD. That is not the way the bill is currently drafted. I will provide the information in a letter and hope the proper changes will be made.

Second, on page 31 of the OTA report, OTA lists the top selling drugs in 1980 and computes patent life at 16.3 years. The underlying issue of this scientific inquiry into H.R. 1937 is simply whether a small, powerful, well-organized group of special interests using academic foils, public unawareness, until today, and doublespeak, can extend their monopoly control over prescription drugs to the point where generic competition is no longer economically feasible. If 7 years is added to the current estimate for patent life of 18.5 years, H.R. 1937 may achieve this elusive goal of the major pharmaceutical companies.

Sometimes I wonder what all this fuss is about, Congressman. Eighty percent of the generic market is already controlled by branded generics produced by PMA members; the same companies control 80 to 90 percent of the entire pharmaceutical market. We make 20 percent of the generic drugs sold in America, so why all the fuss? Because we are the baseline, Congressman. We demonstrate that competition, innovation, and technology can work. And when the Government or a hospital issue a bid, branded generics or trade products must compete with our price. On the day the patent ends prices drop from an average of $7.50 to an average of $1, a drop of 750 percent.

Price is usually a dirty word in scientific hearings, but it is really the essential truth behind the persistent lie about generic drugs. Congressmen Kastenmeier and Railsback recently asked us to produce, for certain major pharmaceuticals, the price differences inherent in the legal three-tier system of selling the same drugs in the United States. As you can see from the chart, the price differences between brand name and true generic average 775 percent. Between branded generic and true generic the difference is 343 percent. On some products like Librium, off patent for 3 years, Congressman Kastenmeier learned from Congress Watch, that the price differences was 1,500 percent.

That defies logic. Who pays these high prices? Not the hospitals that treat Members of Congress, not municipal hospitals, not private hospitals, not the VA, not the Defense Department. It is the 84 percent of the American drug bill that is paid directly by consumers without being subsidized by Government or private plans. There is a national formulary of interchangeable drugs available to the States to verify that these drugs were identical. If 17 were used, this consumer drug bill would also be substantially reduced as it is already reduced for the Government and the military. If H.R. 1937 is passed, these Government savings will evaporate.

Governor Reagan recognized this in California. Governor Laxalt recognized it in Nevada. HEW Secretary Caspar Weinberger recognized it for the U.S. Government mandating generics for medicaid reimbursement, a policy approved by President Nixon. Those are the Republican heroes of generic legislation. On the other side were Kefauver, Long, Nelson, Kennedy, Metzenbaum, and Senator Gore.

Extension of patent terms would change all that has been accomplished in the last 25 years. In the last few months I have walked into one Congressman's office after another trying to make our case. In these meetings I have been met with three succinct arguments. First, if you are right, how come the old people are not with you? Second, do you not agree that patent life should be restored if it was cut in half by the requirements of the Kefauver Act of 1962? Third, it costs $70 million to develop a new drug. Should that investment be protected by patent life?

On the first argument, as you have heard, the American Association of Retired Persons and the National Retired Teachers Association has by unanimous vote of its legislative council, withdrawn its support for this legislation. In doing so they join with the National Council of Senior Citizens in opposing the legislation. Two, and I hope you will listen to this carefully, the argument that patent life was cut in half is directly traceable to a four-page summary of an unpublished study not subject to verification and not due to be completed or filed until the end of this year, and produced by an academic center which receives most of its financing from the very companies who would benefit from this legislation. I would like to introduce into the record a letter sent by that institution which arrived in the offices of a Congressman when this legislation was being considered and is the support for that legislation.

[The letter follows:]

THE UNIVERSITY OF ROCHESTER
SCHOOL OF MEDICINE AND DENTISTRY
601 ELMWOOD AVENUE
ROCHESTER, NEW YORK 14642

CENTER FOR THE STUDY OF
DRUG DEVELOPMENT
(716) 275-2466

DEPARTMENT OF
PHARMACOLOGY AND TOXICOLOGY

March 1981

MEMO from: William M. Wardell, M.D., Ph.D.
Director

The Center is proud to enclose two reprinted articles for your consideration.

The first article is a recent study performed at the Center by Dr. Martin Eisman and myself, "The Decline in Effective Patent Life of New Drugs." This article is particularly timely because of the increased concern -- including legislative attention -- that is currently being focused on the role of patent protection in maintaining incentives for investment in innovative research. We believe this is the first study to analyse the components of effective patent life for drugs, and to identify the relative contribution that each component has made to the decline in effective patent life over the past 15 years. We found that, in the case of the 4-year decline in EPL that occurred from 1968 to 1979, 60% was due to an increase in the clinical/regulatory (IND/NDA) period, while the remainder was due to two other factors not previously considered important: increased (preclinical) time from patent application to first clinical testing in the U.S., and quicker issuing of the patent by the Patent Office.

The second article is by Professors David L. Sackett and Michael Gent, from the New England Journal of Medicine, "Controversy in Counting and Attributing Events in Clinical Trials." This gives a fascinating discussion of the controversy between clinicians, statisticians and others about how patients and outcome events should be counted in the design and analysis of randomized clinical trials. The issues of this controversy affect some current trials, and will undoubtedly become more important in the future.

We also enclose a brochure announcing our 1981 Postgraduate Course in Clinical Pharmacology, Drug Regulation and Development, which is being held this year from November 8th-13th. Please bring this notice to the attention of persons you feel might be interested in our course, and call this office for additional copies if needed.

Finally, we wish to draw your attention to a national conference on "Proper Prescribing: Conflicting Signals," being held in New York City this May 18th and 19th, designed to characterize prescribing and to propose modifications of prescriber behavior. For further information and registration forms, contact the organizer of that conference, John P. Morgan, M.D., at the Sophie Davis School of Biomedical Education, City College of New York J903, Convent Avenue at 138th Street, New York 10031 (212) 690-8255 or 368-6258.

Once again, we hope the enclosed articles will serve to stimulate your interest, and we invite you to share your comments.

Mr. **Gore**. I would like to hold the record open at this point for a response to that statement from the institution.

Mr. **Haddad**. I notice the institution gave you 272 pages, but the budget was not included. I think that might have been an oversight.

Mr. **Gore**. In fairness, the statement did indicate that there had been some industry conclusions as part of the—to the operations of the center. I do not think they have——

Mr. **Haddad**. As you have been fond of saying today, Congressman, it is not the mean that counts, it is the specific. How much did industry put into that institution? This is not new to us. We have had that academic ruse used before, but I am willing to naively accept, in this instance, because of the individuals involved, that in this instance an honorable study was put to dishonorable use. Apples were sold as oranges.

We in the generic industry are experts on patent law. If one of our companies can get into the market first, it captures the greatest market share and realizes distinct economic advantages. We scout patents every day of the week. We know when we can compete without litigation. Therefore, the claim that patent life has been cut in half came as a surprise to us.

Today's hearing may have produced legal business for Mr. Hutt. Every time we are challenged in the courtroom, we will put him on the stand to repeat what he said today about how patents work. Our own investigations showed, as Mr. Larsen indicated to you, that on a $1.3 billion worth of product in 1980 patent life was 18.5 years. Why? Overlapping patents.

We just cannot get into the market to compete. We pleaded with the Congress, with OTA, with PMA, with everyone, to please conduct a study to ascertain the facts. What was the patent life in 1962, when Kefauver and Harris walked into the melee, and what is it today? Put those two numbers up, and if we lose, we will sit here with PMA and say we support patent restoration. We are not against patent life. We are for it, but not for adding patent life that is not deserved or justified by the facts.

I had the opportunity to question the researcher who produced the $70 million figure. What I say is verifiable through the OTA. The researcher said to me that his report did not say $70 million, but $54 million. And his survey had accurately been escalated for inflation to $70 million.

"Did all the companies participate in your survey," I asked?

"No," he said, "only those who chose to do so."

"Did they provide you with all the drugs and all the prices?"

"No," he said, "only those drugs they choose to provide me."

"Can you provide me with a verification so that we can do a third-party study?"

"No," I cannot. I am bound by confidentiality to these companies."

If I turned in such a report in college, the same professor would have flunked me. The essence of academic research is independent verification. Why not here? Especially when the study is being used to turn over a 200-year-old law that has worked so effectively in enhancing innovation in America and finding the balance that Al Engelberg discussed.

Let me offer for your consideration a statement made by Senator Long before the Senate on February 10, 1966. He was reporting on a tetracycline cartel which both the late Senator Kennedy and your father, Senator Gore, were anxious to expose. One company was making lifesaving tetracycline at a cost of 1.6 cents per capsule, and selling it for 51 cents. The drug companies argued they needed those extraordinary profits for research, but Senator Long said they spent 6.4 percent of industry's dollar on research, and for every 6 cents they spent on research they spent a quarter on marketing.

Let me bring that up to date in an attachment. From 1958 to 1977 one company invested $10 million in research and development of cephalexin, a product which won its NDA in 1971, will not go off patent until 1989. The company spent $12.3 million during the first 2 years to promote that drug.

You do not read those numbers in these academic studies. It is in a court record of the company's testimony.

We are trying to get Congress to conduct an independent study which will determine whether we are right or the PMA is right. The issues to be resolved are critical to the survival of our industry.

All this week I have been involved with solving one problem: How to restore the painkillers for arthritic drugs which have been taken off certain State medicaid lists. That means that a patient today, an old patient, one of your constituents, has to choose between a painkiller and fuel. Yet, if you take the eight most frequently prescribed drugs, and use that three-tier system to find out the lowest price permissible under their State law, you would learn the States can save more than $215 million on these eight drugs alone. That means you could include everybody in President Reagan's safety net. The truly needy could be taken care of, and it would not cost the Congress a penny, but it is not happening. Why?

I guess I do not want to disguise my anger any more than Mr. Walker wanted to disguise his this morning. This has been going on for 25 years, and it will go on for another 25 years unless somebody answers the basic questions asked today. One basic question is why would anyone in his right senses would pay seven times more than needed for an identical drug? Finally, let me sum this up with the anecdote which brought me here today.

I was attending a Wall Street conference where someone speaking for President Reagan's Health Task Force, said that "The 20 years of dark clouds that have hung over this industry are about to dissipate, Kefauver is dead, Long is bored, we beat Nelson, and Kennedy is defanged." And when a young man got up and asked, "What about the House of Representatives," he was told, "We do not have any worry from that quarter." Until today I was inclined to agree.

Thank you.

[The prepared statement of William F. Haddad follows:]

Testimony of William F. Haddad, President,
Generic Pharmaceutical Industry Association

Before Committee on Science and Technology,
Subcommittee on Investigations and Oversight

Thursday, February 4, 1982

Congressman Gore, I appreciate the opportunity of appearing before your subcommittee today. As you may know, I have been involved, directly and indirectly, with the issue of providing the consumer and the government lower-priced pharmaceuticals since my association with the late Senator Kefauver of your state.

He regarded this dispute -- which is in its 25th year -- simply as a conflict between the public interest and vested special interests, and, in the instance of this testimony, I share those views and concerns

When you clear this room of publicity men, advertising agencies, hired academics and lawyers, the issue is clearly this: What is it that induces consumers and governments to pay higher prices for identical drugs which are readily available at a fraction of the price? The situation continues to defy gravity. And logic.

The underlying issue of this scientific inquiry into H.R. 1937 is whether a handful of powerful, well-organized special interests can, using academic foils and public unawareness, extend their monopoly control over prescription drugs to the point where generic competition is all but eliminated. If the seven years allowed under H.R. 1937 is added to the loopholes in patent law, that goal may well be achieved.

Ironically, some of those sponsoring this legislation argue that it will help small business. We could do without their kindness.

The trade name companies now control, through high-priced branded generics, some eighty percent of the generic market. You might wonder if we only control 20 percent of the generic market, why all the fuss? I believe it's because we are the baseline. We demonstrate what competition, innovation and technology can do. If it weren't American companies, it would be foreign companies. And when the government, or a hospital, issues a bid, branded and trade name products must compete with our prices.

Price is the dirty word never uttered at scientific hearings, like this, but is the essential truth behind the persistent lie. Congressman Kastenmeier asked us to produce, for certain major pharmaceuticals, the differences inherent in the illogical three tier pricing system for prescription drugs. As you can see on our chart, the price difference between the brand name and the true generic averages 775 percent. Between the branded generic and the true generic, 343 percent. On some products, like Librium, off patent for three years, the difference is 1500 percent.

Who pays these high prices? Not the hospitals that treat Members of Congress. Not municipal hospitals, nor private hospitals. Not the VA. And not the military. But 84 percent of the U.S. drug bill is paid directly by consumers without subsidy from government.

If we had a National Formulary of Interchangeable Drugs, available to the states, this consumer drug bill could also be substantially reduced. Governor Reagan recognized this in California. Governor Laxalt recognized it in Nevada. HEW Secretary Casper Weinberger, under President Nixon, recognized and implemented it in the Medicaid reimbursement program.

Extension of patent terms would change all that has been achieved by these men and others like Kefauver, Long, Nelson, Metzenbaum, and Kennedy.

I have, in the last months, walked into one Congressman's office after another's, trying to make our case. In those meetings, I have been confronted with three succinct arguments:

First, if you are right, Haddad, how come the old people are not with you?

Two, don't you agree that patent life should be restored if it was cut in half by the requirements of the Kefauver-Harris amendments of 1962?

Three, it costs $70 million to develop a new drug. Shouldn't that investment be protected by patent life?

On the first argument, the American Association of Retired Persons and the National Retired Teachers Association has, by unanimous vote of their legislative council, voted to oppose patent extension. It reversed an interim decision.

Two, the argument that patent life was cut in half is traceable to a four-page summary of an unpublished study not subject to verification, and not due to be completed and filed until the end of this year, and produced by an academic center which receives most of its financing from the very companies who would benefit from this legislation.

That type of academic ruse has been used on us before. When we tried to repeal the state antisubstitution laws, instigated by an offshoot of the PMA in the fifties, we were confronted by the same academic veneer which contended that generics, somehow, were not as safe or as effective as trade name products. In my state, New York, these academics met secretly with Members of our Legislature to throw their degrees behind these discredited arguments. I am willing to naively accept, in this instance, that an honorable study was put to dishonorable use.

We in the generic industry are expert on patent law. If one of our companies can get into the market first, it captures the greatest market share and realizes distinct economic advantages. As serious businessmen, we scout patents every day of the week. We know when we can compete without litigation. Therefore, the claim that patent life has been cut in half came as news to us.

Our own subsequent investigation showed that actual effective patent life on 1.3 billion dollars of product in 1980 was 18.5 years. How could that be possible? Because there are multiple patents on products and broad patent claims which are used to legally forestall competition beyond what the Congress intended. We have been the victims of the patent process, not the 15 multinational pharmaceutical companies that OTA says will benefit from patent extension.

We pleaded with the Congress and the OTA to take the PMA claims, fortressed as they were by academia, and compare them to our numbers, and come to their own conclusions. That has not happened. Too many people -- if you will permit a moment of candidness -- were frightened of the results. We have told the PMA, which, literally, drafted this legislation, that we could support some form of patent extension if they could prove their case, because our membership, by and large, would accept a flat 17-year effective patent life beginning with the application for the NDA. The PMA has not yet made its case to us. And, we're still waiting for a report on bottom line, actual effective patent life.

On the third point, the argument is again from an academic, but one I had a chance to question at a recent OTA seminar. What I repeat here is possible to verify with OTA.

The researcher said that it was not $70 million to bring a drug to market, but $54 million; his survey had been escalated, accurately, for inflation.

Did all companies participate, I asked.

No, he said, only those who chose to do so.

Did they provide you with all their drugs?

No, they did not.

Can you provide the raw data for third-party verification?

No, I cannot, he said, I am bound not to do so by the companies supplying the information.

If I turned in such a report in college, I would have flunked this course. The essence of academic research is independent verification. Why not here, especially when it is being used by the Congress to overturn a 200-year-old tradition?

Let me offer for consideration the statement made by Senator Long, before the Senate on February 10, 1966. He was reporting on a tetracycline cartel which both the late Senator Kefauver and your father, Congressman Gore, were anxious to expose. One company was making lifesaving tetracycline at a cost of 1.6 cents per capsule and selling the tablet for 51 cents.

The drug companies, then, as now, argued that they needed the huge profits for research, but Senator Long said research only cost 6.4 percent of industry's dollar and for every six cents the industry spent on research, it spent a quarter on marketing.

An old case. Sure. But it continues. From 1958 to 1977, one company invested $10 million in the research and development of cephalexin, a product which won its NDA in 1971 and won't go off patent until 1989. The company also spent $12.3 million during the first two years the new drug was on the market for a variety of activities designed to promote the prescribing of the drug. You can read those numbers in a judge's decision but not in the study being used to the Congress to justify this legislation. I will include the judge's statement of facts, taken from the company's testimony, for the record.

Why aren't we trying to find out in an independent fashion what it costs to develop a new product? We have the means -- the subpoena if necessary -- and certainly the Congress can be as trusted as an academic. Put the data into a computer and let's see what comes out. Maybe the companies are right. But what it they aren't right?

This story would be incomplete if I did not add the finale. Even after patent protection ends, the brand name company maintains an 80 to 90 percent share of the market at the higher price.

Congressman, in these times of economic crunch, I am sure you know how that translates into human terms. Some states have now cut arthritic pain killers from their Medicaid reimbursement lists. With reduced budgets, something had to give. That means an elderly person must now choose between paying for heat or to curtail pain, a triage decision that should not be required in a democracy like ours. And this need not happen if physicians, influenced by the crude advertising you see here, were not avoiding prescribing the low-priced p prescribed drugs, [illegible] savin be more than $215,[illegible]000. Th his or her pain killer, and go safety net to catch the truly and it will get worse if this through the Congress without i

Sure, Congressman, I'm ang anymore, play the game anymore months ahead, we are going to depend on the government for m safety net and into the arms o Dicken's America. And it need The money saved, under law, ca truly needy.

This legislation, and thi of inquiry. But who is going what happened to him when he t head of the PMA, talking for t the name of a man, Reagan, who with medicines in California, dark clouds which have hung ov were about to dissipate.

"Kefauver is dead," he sa and Kennedy is defanged." And got up in the audience and ask Representatives?" He was told that quarter."

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New York Times

June 9, 1981

City Places Cost of Disregarding Generic Drug Law at $10 Million

By EDWARD A. GARGAN

Consumers may have paid $10 million more than they had to for prescription drugs last year because the state's generic-drug law was not complied with, New York City's Commissioner for Consumer Affairs charged yesterday.

"Doctors' prescribing practices may have cost New York City consumers $8.5 million last year," the Commissioner, Bruce C. Ratner, said. He added: "Not only are many pharmacists possible lawbreakers, but their practice could also be costing New York City consumers $1.5 million a year."

He said the costs stemmed from the fact that doctors were failing to prescribe cheaper generic drugs where possible and that in many cases pharmacies were not complying with the orders for generic drugs when they were signed for.

Under New York State's three-year-old generic drug law, a pharmacist must substitute a generic drug for a more expensive brand-name prescription drug if the doctor indicates on the prescription form that such a substitution is permissible.

The charges by Mr. Ratner follow a citywide survey made last year of 42 pharmacies and 4,200 prescriptions. The results of the survey were released by his office yesterday.

Prescription forms now permit a doctor to sign on one line if he wishes the pharmacist to dispense the brand-name drug or on another line if he wants a generic drug to be used to fill the prescription. Under the law, pharmacists must provide a generic drug if the physician signs the second line.

But, according to Mr. Ratner, in 32 percent of the cases studied, pharmacists failed to comply with the law and dispensed the higher-priced brand-name drug. The commissioner also said that in the case of 42 percent of the prescriptions examined, doctors failed to sign the prescription so that a less expensive generic drug could have been substituted for the brand-name drug prescribed.

A bill designed to encourage greater use of generic drugs in favor of brand names is before the Legislature in Albany. The measure, sponsored by Assemblyman Alexander B. Grannis, Democrat of Manhattan, has encountered stiff opposition from pharmaceutical manufacturers.

The average cost of a prescription for a brand drug in the city is about $6.50, the commissioner said, with a similar prescription with a generic substitute averaging $1.97 less.

"Patients should look at prescriptions from doctors and emphasize to doctors that they want a generic drug," Mr. Ratner said. "Doctors not writing prescriptions for generic drugs are not really helping their patients."

Pharmacies that fail to comply with the generic-drug law are subject to fines and the revocation of their licenses by the State Board of Pharmacy.

COMPARATIVE DRUG PRICES

Generic (Brand Name) Drug Products	Brand Name Price	Branded Generic Price	True Generic Price	True Generic vs. Brand Name % Increase	True Generic vs Branded Generic % Increase
Dipyridamole (Persantine) 25 mg./100s	$ 11.42	$ 6.85	$ 2.20	519%	311%
Isosorbide Dinitrate (Isordil) 5 mg./1000s	51.58	24.20	4.35	1185%	556%
Amitriptyline HCL (Elavil) 25 mg./1000s	73.53	44.90	12.60	583%	356%
Chlordiazepoxide HCL (Librium) 10 mg./500s	43.65	10.55	5.20	839%	202%
Tolbutamide (Orinase) 500 mg./1000s	91.58	52.05	22.95	399%	226%
Hydralazine HCL (Apresoline) 25 mg./1000s	66.07	27.07	7.80	847%	347%
Isoxsuprine HCL (Vasodilan) 10 mg./1000s	137.74	69.44	13.05	1055%	532%
Meclizine HCL (Antivert) 12.5 mg./1000s	61.76	17.06	7.95	776%	214%
	AVERAGE % INCREASE:			775%	343%

Source: Manufacturers'Catalog Prices to Pharmacists

POTENTIAL SAVINGS WITH TRUE GENERICS

Generic (Brand Name) Drug Products	Use	Brand Name Sales 1980 (millions)	Equivalent Generic Cost (millions)	Possible Generic Savings (millions)
Dipyridamole (Persantine) 25 mg./1000s	Coronary	$58,937	$11,356	$47,581
Isosorbide Dinitrate (Isordil) 5 mg./100s sublingual	Coronary	54,102	4,566	49,536
Amitriptyline HCL (Elavil) 25 mg./1000s	Anti-depressant	29,613	5,079	24,534
Chlordiazepoxide HCL (Librium) 10 mg./500s	Anti-anxiety	27,675	3,299	24,376
Tolbutamide (Orinase) 0.5 gm./1000s	Diabetes	22,637	5,673	16,964
Hydralazine HCL (Apresoline 25 mg./1000s	Hypertension	22,441	2,649	19,792
Isoxsuprine HCL (Vasodilan) 10 mg./1000s	Arteriosclerosis	19,101	1,811	17,290
Meclizine HCL (Antivert) 12.5 mg./1000s	Vertigo	17,173	2,213	14,960
TOTALS		$251,679	$36,646	$215,033

Judge's Statement of facts

name "Loridine." These drugs were effective antibiotics only when administered intravenously, however, because they were not sufficiently absorbed into the blood stream from the digestive tract to make oral administration feasible. Consequently, Eli Lilly began experimenting with the side chain attached to the 7-ACA cephalosporin nucleus in order to construct an orally effective form of cephalosporin. It achieved this goal by substituting a phenylglycine side chain at the 7-position. The company's research consultant, Edwin H. Flynn, who was extensively involved in the research, has stated that this result was surprising because identical experimentation with the penicillin nucleus had made that drug active against Gram-negative bacteria — a trait that cephalosporins already possessed.[9] The first orally administerable cephalosporin was called cephaloglycin and was marketed in 1970 by Eli Lilly under the trademark "Kafocin."

Cephaloglycin was found to be eighteen to twenty-two percent absorbed into the bloodstream, which is a sufficient percentage to be a satisfactory oral antibiotic. More than half of the cephaloglycin absorbed, however, underwent a chemical conversion that substantially diminished one of its most useful properties — effectiveness against Gram-negative bacteria.

In the course of the search for an orally administerable cephalosporin that also retained its activity against Gram-negative bacteria, two researchers at Eli Lilly, Dr. Robert E. Morin and Dr. Billy G. Jackson, discovered a novel chemical reaction by which various penicillins could be converted into a type of cephalosporin compound that contains a methyl group at the 3-position in place of the acetoxymethyl group that naturally exists at that position of the cephalosporin nucleus. Although the 3-methyl cephalosporin, unlike cephaloglycin, underwent no chemical changes upon absorption, and therefore remained completely active against Gram-negative bacteria, the scientists found that the drug displayed a markedly lower level of activity than corresponding cephalosporins that contain the natural acetoxymethyl group. As a result, Eli Lilly directed its research away from 3-methyl cephalosporin.

Following a series of unsuccessful experiments with other forms of cephalosporin, Drs. Morin and Jackson urged their colleagues to test once again 3-methyl cephalosporin. In 1965, the researchers subjected cephaloglycin to hydrogenolysis to form the 3-methyl cephalosporin that later came to be known as cephalexin. Cephalexin retained the 3-methyl cephalosporin characteristics of being completely active against Gram-negative bacteria and exhibiting a reduced level of activity. However, cephalexin yielded the unexpected property of being absorbed virtually one hundred percent into the bloodstream and completely excreted in the urine without chemical alteration. The one hundred percent absorption rate more than offset the reduction in the level of activity.[10] As a result, cephalexin is a highly effective oral antibiotic.[11] Eli Lilly obtained a patent for cehpalexin on April 21, 1970.[12] It is the question of the validity of this patent that is before us today.

C. Eli Lilly's Production and Marketing of Cephalexin

From 1958 to 1977, Eli Lilly invested approximately $10 million in the research and development of cephalexin. The research included the chemical synthesis experiments described above, "laboratory evaluations in vitro and in vivo, development of analytical methods, development of processes for the production and purification of cephalexin monohydrate as a chemical product, [and] animal and human pharmacology and metabolism studies."[13] From 1968 to 1977, Eli Lilly spent more than $1.8 million on clinical testing of cephalexin on human beings. A substantial portion of this sum was used to fund studies required by the United States Food and Drug Administration (FDA). Eli Lilly spent more than half of the $1.8 million in post-marketing studies that were designed to adduce additional information about the effectiveness and potential dangers of cephalexin.[14]

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[9] Affadavit of Edwin H. Flynn, Nov. 27, 1978, at 8-9, App. 105, 112-13.

[10] The so-called Morin-Jackson process, entitled "Penicillin Conversion Via Sulfoxide," is protected by U.S. Patent No. 3,275,626.

[11] In its original form, cephalexin, although effective when administered orally, was not well-suited for oral consumption. The cephalexin molecule was originally produced at room temperature as a dihydrate. Because the dihydrate crystals were so bulky and fluffy, a full dose could not be put into a single capsule of acceptable size. On drying, the dihydrate crystals are converted into monohydrate crystals. The cephalexin nonohydrate thus formed was also bulky, however, and the crystals tended to pick up a static charge, which made handling and encapsulation impracticable on a commercial basis.

Accordingly, Eli Lilly began searching for an alternative method of producing cephalexin. Dr. Earle Van Heyningen, an Eli Lilly scientist, discovered a process of crystallizing cephalexin monohydrate at temperatures greater than 60 degrees centigrade such that the crystals obtained were relatively large, nonhygroscopic, dense, and nonelectro-statically excitable. These crystals could be encapsulized relatively easily, and were small enough so that a single dose would fit into a capsule of acceptable size. The patent for this dense form cephalexin was issued on April 11, 1972. U.S. Patent No. 3,655,656. See note 2 supra. Eli Lilly markets most of its cephalexin in this form under the trademark Keflex.

The patent for dense form cephalexin (the '656 patent) is premised on the validity of the patent for regular cephalexin (the '861 patent) which is at issue in this case.

[12] U.S. Patent No. 3,507,861.

Eli Lilly has been quite successful in marketing cephalexin. Cephalexin has become the most widely prescribed oral cephalosporin in the United States, and is the most common substitute for oral penicillin administered to penicillin-allergic patients. Moreover, because of its greater absorption rate, cephalexin generally competes well against ampicillin, penicillin, and other cephalosporins.

D. The Response of the Pharmaceutical Industry to Ely Lilly's Patent on Cephalexin

In general, the other members of the domestic pharmaceutical industry appear to have been interested in selling cephalexin, but to have refrained from challenging Eli Lilly's patents. From 1970, when the first patent on cephalexin was issued, until 1977, Eli Lilly was the sole seller of cephalexin in the United States. During that period, two small domestic drug companies sought to obtain licenses to manufacture cephalexin, but Eli Lilly denied their requests. Four multinational pharmaceutical companies that manufacture cephalexin abroad or have the capacity to produce it here thus far have respected Eli Lilly's patent. None of these companies has a license or other agreement with Eli Lilly that would be jeopardized by an attempt to enter the United States cephalexin market.[15]

Zenith Laboratories, Inc., a domestic producer of generic drugs, began marketing cephalexin in this country in 1977. Zenith produced very little of the drug itself and obtained most of its supply from an Italian manufacturer. Following the issuance of a preliminary injunction against such sales, however, Zenith voluntarily withdrew from the market.[16]

In August or September 1978, Premo advised Eli Lilly that it had obtained large quantities of cephalexin from foreign manufacturers, had put cephalexin into dosage-sized capsules, and was planning to sell the drug in the United States. Premo also stated that it believed Eli Lilly's patent on cephalexin was invalid and therefore unenforceable. In response to this information, Eli Lilly brought the present action to declare the patent valid and to enjoin Premo, preliminarily and then permanently, from selling cephalexin in the United States.

II. Issues Presented On Appeal

On this appeal, Premo raises a number of related contentions. First, it argues that the district court erred in holding that, although structurally obvious in light of prior art, cephalexin was nevertheless patentable because it yielded the unanticipated and nonobvious characteristic of one hundred percent absorbability into the bloodstream. Second, it urges that, even if the district court did not so err, Eli Lilly's patent is invalid because the company did not adequately disclose the absorbability trait in either the patent or in the patent application. Third, it claims the patent is invalid because Eli Lilly disclosed the trait in an amendment to the original Abstract of Disclosure in violation of the statutory prohibition against introducing new matter by amendment. Fourth, it maintains that the patent is invalid because the unexpected property in fact was discovered by someone other than the persons listed in the patent application as the inventors. Fifth, it disputes the district court's conclusion that other domestic drug manufacturers acquiesced in Eli Lilly's patent on cephalexin. Sixth, it contends that the district court abused its discretion in granting the preliminary injunction. We shall address these claims seriatim.

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[13] Zenith Laboratories, Inc. v. Eli Lilly & Co., 460 F Supp. 812, 816-17, 201 USPQ 324, 327-328 (D.N.J. 1978).

[14] In addition, during the first two years of distribution, Eli Lilly expended approximately $12.3 million on a variety of activities designed to promote the prescribing by physicians of cephalexin.

[15] Zenith Laboratories, Inc. v. Eli Lilly & Co., 460 F Supp. 812, 818, 201 USPQ 324 (D.N.J. 1978).

[16] The injunction covered only the patent on dense form cephalexin (the '656 patent). See notes 2 & 11 supra.

APPENDIX "B"

Drug Product	Patent Number	Issue Date	Expiration Date
Aldomet	2,868,818	1959	1976
	3,158,648	1964	1981
	3,230,143	1966	1983
	3,344,023	1967	1984
	3,347,752	1967	1984
	3,517,057	1970	1987
	3,526,698	1970	1987
	4,038,411	1977	1994
Diabinese	3,013,072	1961	1978
	3,121,102	1964	1981
	3,211,615	1965	1982
	3,349,124	1967	1984

APPENDIX "C"

MARKET PROTECTION OF DRUG PRODUCTS

Drug Product	1980 Sales (millions)	NDA Approval	Patent Expiration	Years of Market Protection
Dalmane	$47	1970	1989	19
Ovral	$47	1968	1982	14
Timoptic	$45	1978	1988	10
Tranxene	$40	1972	1987	15
Minipress	$38	1976	1987	11
Haldol	$35	1967	1986	19
Sinequan	$35	1969	1986	17
Nalfon	$32	1976	1988	12
Talwin	$30	1962	1983	21
Ativan	$29	1977	1986	9
Catapres	$25	1965	1982	17
Bactrim DS	$23	1978	1993	15
Valisone	$21	1967	1984	17
13 products	$447			15.1 average years
Top 25 drugs	$1,818			16.7 average years

THE NEW YORK TIMES
May 17, 1981

APPENDIX "D"

The Drug Business Sees A Golden Era Ahead

Hit on a Tagamet, and the money rolls in. New funds are pouring into research. Do science and Reagan spell an end to 'drug lag'?

BY THOMAS C. HAYES

THE Warner-Lambert Company, a major pharmaceutical concern, earned a respectable 13.3 percent on shareholder investment last year, just a shade below the national average for manufacturers of all stripes. But in the exceptionally profitable pharmaceutical industry, it was an also-ran.

Warner-Lambert and its fellow also-rans now have a chance to recoup. With the expectation of increasing demand for a host of new drugs for an aging population, with early signals that the Reagan Administration will relax regulatory requirements, and with such dramatic advances as interferon research in the biological sciences, the drug industry may be on the brink of even greater profitability.

"These factors will make the 1980's a golden age of drug research," Ronald M. Nordmann, senior drug analyst at Oppenheimer & Company, said. "You will see more interesting new drugs in the 1980's than any decade within memory."

This is the industry of the Big Breakthrough, where the introduction of one successful product can literally make a faltering company whole or pay for an expensive research program many times over. No one knows this better than the SmithKline Corporation, whose stock has multiplied eightfold since 1975, the year before its ulcer remedy, Tagamet, was introduced. Profits from Tagamet, which last year passed Valium as the world's largest-selling prescribed drug, have helped catapult SmithKline into the big-spending race to create new cures.

The drug manufacturers, in addition to seeking speedier Government testing, are already lobbying for extension of drug patents to hold on longer to exclusive rights on best-selling drugs. And virtually all of them are planning higher outlays for research.

In the 70's, companies like Warner-Lambert suffered by comparison because they were slow to commit funds to aggressive research. "We have not had the most productive history in developing new compounds," Donald E. O'Neill, president of Warner's Parke-Davis pharmaceutical division, acknowledged in an interview.

This year, though, reflecting an outlook that has become close to gospel across the pharmaceutical business, Warner allocated about $80 million of its overall $120 million research budget to Parke-Davis. The 20 percent increase is typical of big and small companies alike. Warner, meanwhile, is hoping to strike it rich with Lopid, a hypertension drug awaiting approval from the Food and Drug Administration. A success with Lopid would bring in large amounts of cash that could further support research.

Best-selling drugs like Tagamet can tally $5 billion in sales in 10 years on an investment of roughly $40 million. Such discoveries can transform a dull, frustrated company into the envy of its peers.

"The name of the game continues to be getting the big product to come along and have an important effect on sales and earnings," Neil P. Sweig, health care analyst with Shearson Loeb Rhoades Inc., said.

Companies are using advances in molecular biology and computer science to concentrate their research on drugs that have a wide potential application. Before, research was more of a hit-or-miss screening of unproven compounds. Today, the biggest efforts are being mounted for drugs to treat heart disease, hypertension or high blood pressure, arthritis and the varieties of aches and pains associated with advancing age.

Restrictions by the F.D.A. have continually narrowed the number of new drugs approved each year. Under the Reagan Administration, a general move toward deregulation is expected. No one, however, is predicting a return to the days before 1963 when drug manufacturers had only to establish that a new drug was safe before it was approved for general use by physicians. Since then, manufacturers have also had to prove that their new drugs actually worked. From a high-water mark of 65 new drug introductions in 1959, the figure dropped to 12 last year. Top researchers in the major drug companies, like Merck & Company, Pfizer Inc. and Eli Lilly & Company, and industry analysts are reluctant to say how much they expect the so-called drug lag to abate. Most believe it will.

"People have seen the importance of new products and their specific, positive effect on human health," said Dr. P. Roy Vagelos, a physician who heads Merck & Company's research arm, Merck Sharp & Dohme Research Laboratories. "It's also fair to say there will be a significant increase in new drugs because of what has happened in science," he added.

THE drug companies were once tight-lipped about the secret compounds still submerged in a battery of animal and patient tests mandated by the F.D.A. Today, by contrast, they are more eager to discuss the potential of the drugs. The bidding on Wall Street for pharmaceutical shares is closely tied to the promise of drugs in the pipeline.

"Stocks move on the basis of significant new products," John P. Curran, a specialist in pharmaceutical economics at Wood Gundy, said. "A stock will explode on news of big prescriptions after a new drug is introduced."

Merck created a stir on April 1 when it announced that a new drug, Timolol, reduced deaths among 186 patients who had suffered recent heart attacks by 39 percent. The company's shares jumped 4[illegible], to 89[illegible], that day, and subsequently reached 96[illegible], closing Friday at 93, up 2[illegible].

Another Merck offering, Heptavax-B, "has the potential to eradicate hepatitis B virus infections, which is uncurable and untreatable, much like measles has been eradicated," Dr. Vagelos said. Both drugs have completed pre-market tests. Merck hopes to manufacture them for sale next year if the F.D.A. approves the drugs.

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Merck, with headquarters in Rahway, N.J., is spending $280 million on research this year, the most of any American pharmaceutical manufacturer. It was the most profitable, earning $415.4 million, with a hefty 13.3 percent profit margin and 22.3 percent return on equity.

"Merck has always been the premiere research house in the United States," Mr. Nordmann of Oppenheimer said. "But it went through a very dry period, from 1965 to 1975. It now appears they are back on stream with an overabundance of new products that are about to be introduced."

Although Merck might have appeared dormant, it did not cut back on research, according to Dr. Vagelos. "Many of the drugs that are breaking the surface now were in the pipeline during that time," he said.

It's true that a company never knows when research will be successful. "But, as these biological processes are elucidated better and better," said Marsha H. Fanucci of Arthur D. Little Inc., a consulting concern, "it will allow companies to be more technologically and philosophically sophisticated."

The first signs are already apparent, research executives say. "The main impact of the new biology is making itself felt now at earlier stages of investigation for new compounds," Dr. Barry M. Bloom, head of research at Pfizer, said.

As an illustration, Dr. Bloom said Pfizer researchers were able to use gene-splicing methods to quickly identify a drug that appears to sharply reduce deterioration of the nervous sytem suffered by people with severe cases of diabetes.

It took Pfizer three years to identify the compound and another two years for preliminary tests in humans. "I wouldn't want to guess how long it would have taken by random, nonrational searching," Dr. Bloom said. The drug, Sorbinil, was patented in December 1978. Pfizer must complete another study of the drug's effect on dozens of patients before it can apply for F.D.A. approval.

At the end of 1980, it took a drug manufacturer an average of 33 months to obtain approval from the F.D.A. to begin selling a new drug. Pfizer, for instance, has been waiting since March 1978, for approval of Feldene, a once-a-day treatment for arthritis. The drug has been a success in several European countries. Analysts who follow Pfizer expect that Feldene's worldwide sales could eventually top $200 million a year after it is approved in this country.

THE F.D.A. is a unit of the Department of Health and Human Services. It has come under fire from drug manufacturers, who contend that the agency too often drags its feet before completing its review of a new drug application. But the long and expensive path to marketing a drug cuts both ways. Companies with F.D.A. approval to sell a drug have a strong edge over competitors seeking to sell a copy or a slight variation of their innovative drug.

Critics of the pharmaceutical research companies say that keeps drug prices artificially high and unjustly inflates profits. In response to those pressures, the Reagan Administration last month opened the door for the F.D.A. to allow so-called "me-too" manufacturers to cite published tests of the pioneering research companies in compiling their applications, rather than being forced to replicate the costly experiments on their own.

Still, Richard S. Schweiker, the new Secretary of Health and Human Services, is expected to trim the so-called drug lag at the F.D.A. The new head of the F.D.A., Dr. Arthur Hull Hayes Jr., a physician from Pennsylvania, was chosen by Mr. Schweiker. Members of the Reagan Administration are well-acquainted with the drug manufacturers' laments. Mr. Schweiker was an active author of legislation to ease drug regulations when he was a Republican Senator from Pennsylvania.

"The appointment of Schweiker is a big plus for the drug industry," Mr. Nordmann of Oppenheimer, said. "His goal is to eradicate the drug lag. It will cut down on the time and expense of getting a new drug on the market."

Vice President Bush, was a director of Eli Lilly from 1977 to 1979. And Donald H. Rumsfeld, Secretary of Defense in the Ford Administration, is now president and chief executive of the G.D. Searle Company. The F.D.A. has blocked Searle's introduction of a putatively profitable, noncaloric sweetener called Aspartame, since 1974, requiring more tests on possible harmful side effects.

In addition to more expeditious drug reviews, drug manufacturers are seeking extension of patent laws that would guarantee them certain years of exclusive manufacturing and marketing rights for the drugs they develop in their laboratories.

According to the Pharmaceutical Manufacturers Association, the 12 drugs approved in 1980 averaged 10 years in research and F.D.A. review before they could be sold. That left seven years of exclusive sales rights. After that, competing manufacturers will be free to study the research and sell copies of the original drug.

Dr. Sidney Wolfe, a physician who heads the health care unit of Public Citizen, a consumerist lobbying group in Washington, contends that Americans have paid too high a price for prescription drugs. The United States is one of the few countries in which the government does not control the price of drugs.

"It's an industry that is rolling in money," Dr. Wolfe said. He also attacked efforts by pharmaceutical companies to convince Congress to extend drug patents. The manufacturers argue that they are increasingly less able to recoup their research costs, because of the dwindling patent life.

"It's outrageous," Dr. Wolfe countered. "The best-selling drugs have hit as much as $5 billion in sales before the patents come off. Their research is not terribly creative anyway. Most drugs are copies of what is already available. They offer little therapeutic advantage."

In brief, the debate is over how much profit is enough for drug manufacturers, given the risks they assume. They do not publish profit markups on the drugs they sell. But Dr. Wolfe contends that it is not unusual for pioneering drugs to sell at wholesale for seven times the price of generic copies.

"That should give you an idea of the fraction of the wholesale price that is represented by actual cost, including research and development," he said. Drug executives argue that the threat of lawsuits hangs over each of their products, despite what could be an experience of thousands of prescriptions without damaging side effects.

The Pharmaceutical Manufacturers Association, adding the average expense of research gone awry on laboratory failures, puts the average cost of marketing new drugs at $70 million. The risks of unfore-

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seen side effects and related vulnerabilities to lawsuits add to a drug company's expenses. Last year, for instance, SmithKline pulled a new antihypertension drug from the market after reports of liver disorders and some deaths. It has been hit by 30 lawsuits. The drug, Selacryn, was licensed from a French manufacturer.

Despite such vagaries, pharmaceutical companies earned the fourth-highest return on equity in American industry last year, at 20.5 percent, ranking behind the oil services industry, energy companies and the tobacco industry.

Breakthrough drugs contribute most of the profits. Four out of five drugs available never cross the threshold of sales of $20 million a year, according to the Arthur D. Little firm. In some cases, the huge investments and long seed time necessary to execute a successful research program have caused some companies to back away from drugs, according to Richard L. Hughes, a health-care specialist with Little.

"One group says that even if you bring out a wonder drug in 10 years, it may not equal what you could get by simply investing in the money market at 15 percent and waiting 10 years," he said. "Risk and return has become a very important factor."

In the main, however, drug company executives are going with the scientists, putting more money into research today with the hope that more new drugs and bigger profits will blossom at some distant tomorrow.

"All it takes is one hit every three to five years, and you can sustain all the risk," Mr. Sweig, the Shearson analyst, said. ■

NO. 2: **VALIUM**

Valium is no longer the runaway leader among prescription drugs, but the tranquilizer and muscle-relaxant still is among the world's most widely dispensed druggist potions.

Valium rang up about $350 million in sales around the world last year for its creator, Hoffman-La Roche Inc. That trailed the $625 million for Tagamet, the five-year-old ulcer treatment from the SmithKline Corporation.

From a peak of more than 50 million in 1975, Valium prescriptions dipped below 33 million last year. Physicians have been disturbed by patient abuse of the drug, especially when combined with alcohol. Some heavy users also have suffered addiction. The company maintains that Valium's safety under proper dosage has never been in dispute.

A further dip in sales is expected after 1985, when Valium's patent expires. "Valium is being looked at enviously by a number of people," Irwin Lerner, president and chief executive of Hoffman-LaRoche, said in an interview at the company's American headquarters, in Nutley, N.J. The company, which posted $2.5 billion in worldwide sales last year, is based in Basel, Switzerland.

Still, Hoffman-LaRoche has had a huge and steady stream of profits from Valium since its introduction in 1963. It helped bankroll the company's strong position among the small army of companies searching for new drugs, including a cancer cure from an interferon compound. Roche poured $350 million into research last year, the most of any drug company in the world.

"The profits from Valium are footing the bill for our work in interferon," Mr. Lerner said. "We think we have more exciting leads than at any other time in our history."

Some Big Bets Coming to Market

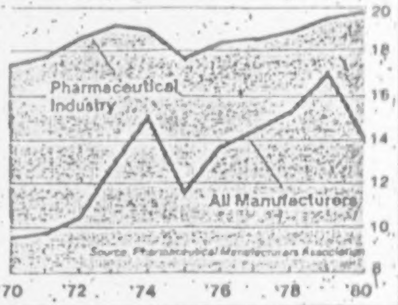
Product	Company	Purpose	Potential Market* (Millions)
Timolol	Merck	Reduces risk of second heart attack	$500 to $1,000
Auranofin	SmithKline	Oral dosage of gold for rheumatoid arthritis	$250
Feldene	Pfizer	Treatment of arthritis	$200
Human Insulin	Eli Lilly	Treatment of diabetes; first big product from genetic engineering	$200
Capoten	Squibb	Treatment of hypertension	$200
Inocor	Sterling	Expected to replace digitalis in treating congestive heart failure	$200

* Potential annual sales, worldwide, at peak of use. *Source: Shearson Loeb Rhoades Inc.*

A Prescription for Profit

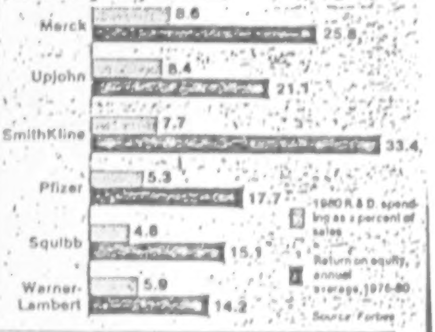
Profitability has consistently been good.

Return on equity, in percent



Source: Pharmaceutical Manufacturers Association

Research is considered the key to profits.



Source: Forbes

The Top Sellers

Ranked by 1980 sales in the United States

Drug	Manufacturer	Disease or Function	Introduced	Sales (Millions)
Tagamet	SmithKline	Peptic ulcers	1977	$250
Valium	Hoffmann-LaRoche	Muscle relaxant, tranquilizer	1966	$230
Inderal	Am. Home Products	Heart disease, hypertension	1967	$200
Motrin	Upjohn	Arthritis	1974	$150
Aldomet	Merck	Hypertension	1963	$150
Dyazide	SmithKline	Hypertension	1965	$145
Keflex	Eli Lilly	Oral antibiotic	1971	$140
Clinoril	Merck	Arthritis	1978	$125

Source: Oppenheimer & Company

APPENDIX "E"

Wall Street report

The Drugs in the Eighties: The Growth Will Be There – Part 1

by James L.L. Tullis

Mr. James Tullis is a principal of Morgan Stanley & Co. Incorporated in New York City. He may be reached at (212) 974-4414

Investors desire certainty, to the extent it can be defined. Yet seldom in recent history have the capital markets reflected as high a degree of uncertainty as they do today. For example, currently the cost of debt capital is both very high and subject to extreme short-term volatility. Moreover, whereas market participants increasingly anticipate recession and disinflation in 1981, economic activity and interest rates continue to be far higher than general expectations.

In this environment, an industry which offers relatively high predictability and which is intrinsically capable of adjusting to a broad range of potential economic scenarios will attract investors. This is particularly true if the fundamental outlook for the business is improving.

STRONG RELATIVE PROFIT PROSPECTS, IMPROVING FUNDAMENTALS

The drug industry's earnings outlook is excellent, both near and longer term, particularly in relation to expected trends in domestic corporate profits. In the 1981 to 1986 period, we expect net income of both ethical and consumer-sensitive pharmaceutical firms to expand more rapidly than in 1975 to 1980. (However, the pickup will be more pronounced in the ethical segment, which is more sensitive to trends in the prescription drug business.)

Specifically, we estimate profits in the ethical drug sector will rise about 12 percent in 1981, while earnings in the consumer-sensitive category expand 5 percent if Warner-Lambert with its large write-offs is included or 10 to 11 percent excluding Warner-Lambert. By contrast, corporate profits are now forecast to rise 3 to 4 percent this year. On an operating basis, the industry's performance should be even more impressive than these earnings projections indicate, because our estimates include the impact of the severe currency-related penalties which all of the heavily multinational drug firms are incurring this year as a result of the dollar's continuing strength. (We think currency factors will reduce drug profits overall by 5 to 10 percent this year.)

In 1982, industry earnings growth should be especially strong. Our preliminary forecasts, as detailed in **Table 1**, call for profit gains of close to 20 percent in both the ethical and consumer-sensitive segments next year. Such increases would outpace the 10 percent advance forecast for profits in general, even in the rapid recovery stage of an economic expansion.

In 1983 to 1986, we anticipate earnings growth in the ethical drug sector will average about 15 to 16 percent per year, which represents a significant premium above the 7 to 8 percent gains projected for corporate profits.

Consumer-sensitive firms should also post net income advances exceeding those of the S&P 400 in that interval, although the expected earnings expansion (12 to 14 percent per annum) will be less rapid than that in the ethical category.

Based on these projections, drug stocks should retain considerable appeal well into the next economic expansion. In addition, the group's investment attractiveness should be enhanced by a number of other factors:

- The liquidity of the pharmaceutical industry remains very high, with almost all firms retaining substantial cash positions which exceed short-term debt and in most cases total borrowings. As a result, three benefits accrue: (1) high short-term interest rates generally help earnings, as interest income more than offsets interest expenses; (2) dividends can be increased faster than profits expand (as was the case in 1979 and 1980); and (3) companies have funds to repurchase stock in the open market, aiding per share earnings comparisons (more than half of the drug firms currently have active stock repurchase programs).
- The drug industry, which has demonstrated its general ability to cope with inflation by raising prices and controlling costs, should also be a significant beneficiary of disinflation. Pharmaceutical firms would begin to feel the impact of diminishing cost increments before the rate of price hikes slowed; thus, margins would improve early on. Importantly, our five-year earnings forecasts for the

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Table 1. Healthcare Industry: Current Earnings Estimates

Industry Segment	Price 5/26	Div. Rate Per Share Cur.	Div. Rate Per Share 12/81	Yield Cur.	Yield 12/81	Earnings Per Share 1979A	Earnings Per Share 1980	Earnings Per Share 1981E	Earnings Per Share 1982E	P/E Ratio 1980	P/E Ratio 1981E	P/E Ratio 1982E	EPS Next Quarter 1980	EPS Next Quarter 1981E	EPS Next Quarter Ending
Hospital Supply															
ABT	56.00	1.44	1.44	2.57	2.57	2.97	3.46	4.05	4.75	16.18	13.83	11.79	0.85	1.00	JUN
AHS	46.00	1.08	1.08	2.35	2.35	2.78	3.03	3.55	4.20	15.18	12.96	10.95	0.76	0.81	JUN
BAX	56.00	0.76	0.76	1.36	1.36	3.02	3.40	3.87	4.63	16.47	14.47	12.10	0.87	0.94	JUN
BDX	47.00	1.00	1.17	2.13	2.49	3.01	3.14	3.55	4.00	14.97	13.24	11.75	0.80	0.88	JUN
MDT	40.00	0.48	0.60	1.20	1.50	2.52	2.80	3.50	4.25	14.29	11.43	9.41	0.80	0.80	APR
Consumer Sensitive															
AHP	34.00	1.80	2.02	5.29	5.94	2.51	2.84	3.20	3.63	11.97	10.63	9.37	0.64	0.71	JUN
BMY	53.00	1.84	1.84	3.47	3.47	3.50	4.08	4.55	5.15	12.99	11.65	10.29	0.97	1.06	JUN
JNJ	106.00	2.30	2.60	2.17	2.45	5.76	6.50	7.35	8.70	16.31	14.42	12.18	1.63	1.86	JUN
MNP	31.00	1.52	1.65	4.90	5.32	3.40	3.52	3.70	4.11	8.81	8.38	7.54	0.56	0.70	JUN
STY	22.00	0.92	1.03	4.18	4.68	1.85	2.04	2.20	2.45	10.78	10.00	8.98	0.42	0.43	JUN
WLA	23.00	1.32	1.35	5.74	5.87	1.55	2.41	0.52	2.50	9.54	44.23	9.20	0.69	0.58	JUN
Ethical Drugs															
LLY	62.00	2.30	2.70	3.71	4.35	4.43	4.52	5.17	6.35	13.72	11.99	9.76	0.98	1.03	JUN
MRK	91.00	2.60	3.00	2.86	3.30	5.06	5.54	6.20	7.40	16.43	14.68	12.30	1.47	1.57	JUN
PFE	48.00	1.60	1.65	3.33	3.44	3.26	3.48	3.70	4.60	13.79	12.97	10.43	0.79	0.79	JUN
SGP	37.00	1.60	1.73	4.32	4.68	4.12	4.45	4.60	5.25	8.31	8.04	7.05	1.20	1.22	JUN
SRL	31.00	0.52	0.52	1.68	1.68	1.68	1.85	2.25	2.65	16.76	13.78	11.70	0.46	0.49	JUN
SKL	83.00	1.92	2.30	2.31	2.77	3.78	4.65	5.70	6.75	17.85	14.56	12.30	1.04	1.27	JUN
SQB	36.00	1.20	1.25	3.33	3.47	2.71	2.65	2.70	2.95	13.58	13.33	12.20	0.50	0.47	JUN
SYN	58.00	1.30	1.60	2.24	2.76	3.77	4.28	5.45	6.35	13.55	10.64	9.13	1.03	1.35	APR
UPJ	63.00	2.00	2.25	3.17	3.57	5.03	5.71	6.25	7.07	11.03	10.08	8.91	1.53	1.60	JUN

E = Morgan Stanley Research Estimate

industry would not be significantly changed if the underlying inflation rate dropped to 6 percent from the 8 to 9 percent level forecast.

- Political and governmental trends, still an important element in the industry's outlook, have become more favorable. Under Reagan Administration directives to reduce Federal red tape, the pace of new-drug approvals should accelerate. Also, the probable attempt to cut down the extremely large existing backlog of pending new-chemical entity applications (as shown in Table 2) could result in a significant short-term spurt in the number of products coming to market. In addition, chances have increased that Congress will eventually pass legislation to extend the duration of patent protection for pharmaceuticals, providing long-needed relief for the industry.
- There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced.
- Although drug stocks have performed well for the past three years, the shares of almost all pharmaceutical companies are inexpensive by historical standards (Figure 1). Since 1946, the multiple premium accorded to the drug companies relative to the S&P 400 averaged about 70 percent, in a range of 20 to 150 percent (excluding one brief period in the early 1950s when the group commanded no premium and two longer intervals in the late 1940s and early 1970s when the stocks sold at price/earnings ratios more than 200 percent above that of the composite). Currently, drug shares are valued about 33 percent and 24 percent above the multiples of the S&P 400 based on estimated 1981 and 1982 earnings, respectively. At the same time, the ratio of the industry's profit growth rate to that of the composite is near peak levels.

WHY ARE DRUG FIRMS DOING WELL?

The current strong and improving fundamental position of the drug industry is best appreciated in the context of past experience. Between 1945 and 1974, pharmaceutical company sales and profits grew, on average, at an annual rate of 10 percent. Earnings gains followed a relatively predictable cycle, expanding as much as 20 percent a year during economic advances and only about 2 percent during economic contractions. From 1975 to 1977, the industry went through a sustained three-year period of laggard (less than 10 percent per annum) profit expansion at a time when many other sectors were

Table 2. New Chemical Entity NDAs Awaiting FDA Approval in the United States

Industry Segment	Estimated New Chemical Entity NDAS Currently Before FDA	R&D Spending 1979	R&D Spending 1980	R&D Spending 1981E
			($ Millions)	
Consumer Sensitive				
American Home Products	4	$ 90.0	$102.0	$116
Bristol Myers	4	103.0	128.0	150-155
Johnson & Johnson	3	192.7	232.8	280
Morton-Norwich*	2	19.2	21.8	24
Sterling	0	48.9	58.1	68
Warner-Lambert	1	94.0	103.0	116
Ethical Drugs				
Eli Lilly	3	177.0	200.7	230-235
Merck	5	188.1	233.9	280.0
Pfizer	5	138.0	160.0	190.0
Schering-Plough	4	75.0	90.0	110.0
Searle	2	59.5	71.3	90.0
SmithKline	0	103.0	136.0	170.0
Squibb (Capoten just approved)	0	69.0	77.0	90.0
Syntex*	1	42.0	54.0	66.0
Upjohn	6	129.3	147.3	160.0

*Fiscal 1979, 1980, and 1981, respectively

Morgan Stanley Research Estimates

registering extremely robust increases. There were several reasons for the relatively disappointing performance of drug firms:

(1) Inflation had accelerated, but pharmaceuticals manufacturers, following a 30-year record of stable pricing policies overall, were loath to increase prices aggressively. At the time, Senator EDWARD KENNEDY was holding regular hearings on industry practices before a liberal, Democratic Congress, presumably hostile to drug company profits.

(2) Unit volume growth was poor (3 to 4 percent a year domestically versus a historical trend of 7 to 8 percent), as only a handful of new products was introduced and as side-effect concerns pared consumption of certain leading products (such as oral contraceptives, tranquilizers, antibiotics, and some analgesics like *Darvon*).

(3) An initial attack on drug prices by many foreign governments hurt foreign earnings just as the sustained three-year strengthening of the United States dollar caused large penalties on the translation of overseas profits into dollars. Drug industry net income still expanded from 1975 to 1977 -- but at less compelling rates than in many prior years and less rapidly overall than earnings of the S&P 400.

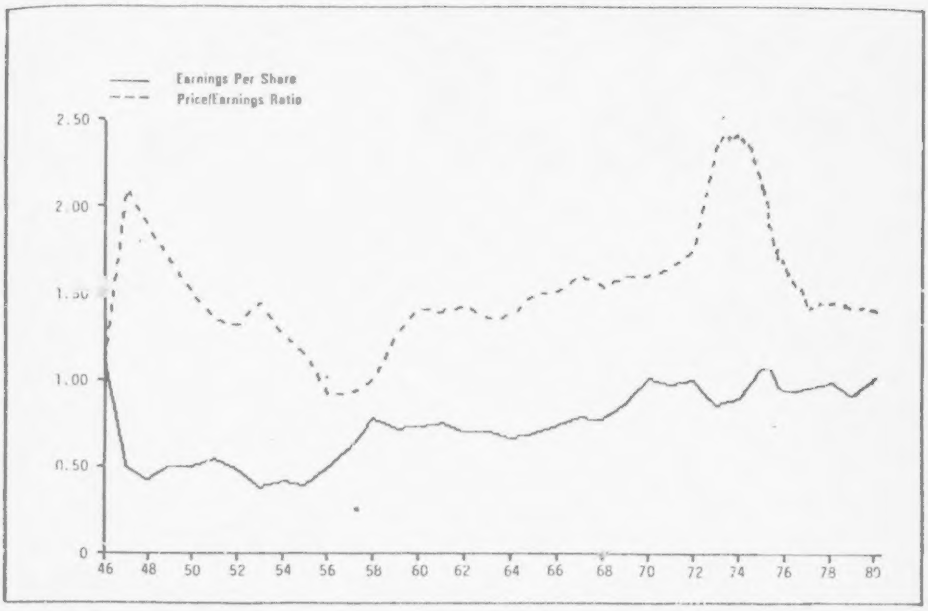
From 1978 to 1980, the industry's vitality improved for several reasons. Drug firms gradually became more willing to increase prices. By 1980, the annual rise in realizations reached 8 to 9 percent, a level since surpassed. Domestically, governmental agencies, which pay for only a very small portion of all drug purchases, and consumers showed no sign of resistance. Senator Kennedy's hearings ended quietly. Unit volume gains were helped (a bit) by new-product introductions. Also, the dollar weakened, and currency impacts became positive rather than negative. Foreign governments learned that drugs represent but a small portion of healthcare costs and are economically efficient; thus, officials gradually began to allow price increases. Tight cost controls put into effect in 1976 and 1977 started to exert a favorable impact on margins. Profit momentum improved, with the industry registering double-digit gains of 19 percent, 15 percent, and 11 percent in 1978, 1979, and 1980, respectively. **Table 3** shows trends in pretax profits in the 1975 to 1980 period and our estimates for 1981 and 1982.

The gains forecast for this year and next are surprisingly strong, especially when one considers that currency trends will probably have a more adverse impact on profits in 1981 than in any prior year while the economic outlook has weakened, with at least a mild recession now expected in the second half of the current year. In the following sections, we will discuss the assumptions used in developing our earnings model.

DOMESTIC MARKET OUTLOOK 1981–1982

We project that overall prescription dollar volume in the domestic market will expand rapidly (up 15 to 17 percent) in 1981 and as fast (or perhaps a bit faster) in 1982.

Figure 1. Standard & Poor's Drug Index Relative to 400 Industrials



Source: Morgan Stanley Research

The potential for further acceleration in 1982 derives from the possibility that the Food and Drug Administration (FDA) will "unjam" the large backlog of new drugs awaiting domestic marketing approval. The primary element in the strong sales growth forecast for 1981 and 1982 (compared with historical 10 percent per annum trendline increases) is higher drug prices. We estimate realizations will rise at a double-digit (10 to 12 percent) rate in 1981 – faster than in any prior year – and 9 to 10 percent in 1982. Our projections for next year assume a slightly slower pace of price boosts, as the Morgan Stanley economic forecast indicates inflation should moderate by then. However, if inflation remains high, we think the rate of drug price expansion will also stay high.

It is important that investors recognize that drug unit demand is not sensitive to price. In many businesses (e.g., autos, soft drinks, and restaurants), the price increases needed to maintain margins during a period of high inflation eventually lead to reduced consumption. However, demand for prescription drugs is uniquely price insensitive because (1) the cost/benefit equation is extremely favorable; (2) the patient has less to do with the purchase decision than his doctor, who is not paying the bill; and (3) the average patient spends only about $40 to $45 per year on prescription drugs – a remarkably small absolute amount. Reflecting these elements, surveys show that consumers have remarkably little awareness of or concern about drug prices. Also, Federal and state government purchases represent a very small (10 percent at most) portion of drug volume, and government (in this country) has no real control over drug pricing.

We forecast unit volume will increase 4 to 5 percent this year, a slightly higher gain than in the past five or six years, but still below the long-term trend. In 1982, we expect unit volume expansion to accelerate to 6 to 7 percent, primarily because of better economic conditions but also because of an increased flow of new products to market. If the FDA can straighten out its approval processes and actually begin to catch up on long overdue approvals, unit volume growth next year might exceed 7 percent. It seems clear that the number of new-drug approvals granted in 1982 will be higher than the 12 of

Table 3. Healthcare Industry: Pretax Earnings (1975-1982)

($ Millions)

Health Industry Segment	Amount								Year-to-Year % Change						
	1975	1976	1977	1978	1979	1980[a]	1981E	1982E	1976	1977	1978	1979	1980[a]	1981E	1982E
Hospital Supply															
Abbott	102.40	138.00	183.40	233.70	282.60	337.66	391.11	451.27	34.77	32.90	27.43	20.92	19.48	15.83	15.38
Amer. Hosp. Supply	97.70	117.70	134.40	147.90	155.00	187.00	222.00	266.00	20.47	14.19	10.04	4.80	20.65	18.72	19.82
Baxter Travenol	55.60	84.50	108.10	119.10	145.00	164.00	192.00	231.00	51.98	27.93	10.18	21.75	13.10	17.07	20.31
Becton, Dickinson*	62.20	75.90	84.40	93.20	102.00	100.00*	110.00	126.00	22.03	11.20	10.43	9.44	−1.96[b]	10.00	14.55
Medtronic**	25.10	23.60	27.80	39.90	53.17	64.80	80.91	102.00	−5.98	17.80	43.53	33.26	21.87	24.86	26.07
Total	343.00	439.70	538.10	633.80	737.77	853.46	966.02	1176.27	28.19	22.38	17.78	16.40	15.68	16.70	18.10
Consumer Sensitive															
Amer. Home Prds.	496.50	544.40	596.40	682.30	751.00	852.00	960.00	1075.00	9.65	9.55	14.40	10.07	13.45	12.68	11.98
Bristol-Myers	257.80	288.70	329.00	375.70	421.00	490.00	546.00	615.00	11.99	13.96	14.19	12.06	16.39	11.43	12.64
Johnson & Johnson	318.80	361.50	432.20	514.20	590.00	675.00	774.00	912.00	13.39	19.56	18.97	14.74	14.41	14.67	17.83
Morton-Norwich***	33.90	7.50	54.60	62.10	76.80	72.96	77.87	87.29	−77.88	628.00	13.74	23.67	−5.00[b]	6.73	12.10
Sterling	145.80	153.50	163.40	183.80	200.00	222.00	235.00	262.00	5.28	6.45	12.48	8.81	11.00	5.86	11.49
Warner-Lambert	289.00	296.00	341.00	362.00	231.00	330.00	125.00	364.00	2.42	15.20	6.16	−36.19	42.86	−62.12	191.20
Total	1541.80	1651.60	1916.60	2180.10	2269.80	2641.96	2717.87	3315.29	7.12	16.05	13.75	4.11	16.40	2.87[c]	21.98[c]
Ethical Drugs															
Eli Lilly	301.50	346.10	394.50	482.50	558.00	590.00	670.00	808.00	14.79	13.98	22.31	15.65	5.73[b]	13.56	20.60
Merck	378.30	416.40	453.50	507.90	606.00	655.00	717.00	853.00	10.07	8.91	12.00	19.31	8.09[b]	9.47	18.97
Pfizer	211.90	237.90	263.60	319.30	363.00	409.00	448.00	557.00	12.27	10.80	21.13	13.69	12.67	9.54	24.33
Schering-Plough	210.50	234.40	241.60	272.70	307.00	326.00	338.00	388.00	11.35	3.07	12.87	12.58	6.19[b]	3.68	14.79
Searle	93.50	89.60	106.10	121.[illegible]	134.00	138.00	167.00	202.00	−4.17	18.42	14.61	10.20	2.99	21.01	20.96
SmithKline	94.20	107.10	134.30	261.30	354.00	446.00	546.00	652.00	13.69	25.40	94.56	35.48	25.99	22.42	19.41
Squibb	134.90	147.40	154.70	150.50	149.00	159.00	171.00	196.00	9.27	4.95	−2.71	−1.00	6.71	7.55	14.62
Syntex	48.90	49.30	46.50	62.90	75.00	89.00	116.00	138.00	0.82	−5.68	35.27	19.24	18.67	30.34	18.97
Upjohn	120.20	128.30	147.60	202.00	204.00	230.00	249.00	291.00	6.74	15.04	36.86	0.99	12.75	8.26	16.87
Total	1593.90	1756.50	1942.40	2380.70	2750.00	3042.00	3422.00	4085.00	10.20	10.58	22.56	15.51	10.62	12.49	19.37
Health Industry Total	3478.70	3847.80	4397.10	5194.60	5757.57	6537.42	7135.89	8576.56	10.61	14.28	18.14	10.84	13.54	9.15	20.19

*Fiscal years ended September 30

**Fiscal years ended April 30

***Fiscal years ended June 30

[a] Results shown are after the effect of change to LIFO accounting by five firms in 1980. Before the effect of these accounting changes, pretax profits and rates of increase of these segments and total industry were: Hospital Supply, $867.76 million, up 17.62%; Consumer Sensitive, $2,653.66 million, up 16.91%; Ethical Drug, $3,126.80 million, up 13.7%; and Industry Total $6,648.22 million, up 15.47%.

[b] After the effect of switching to LIFO Accounting, which reduced reported 1980 results. Had FIFO accounting been used in both years, pretax earnings growth rates would have been, respectively: 10.23% (Morton-Norwich), 12.06% (Becton, Dickinson), 11.68% (Eli Lilly), 13.76% (Merck), and 11.[illegible]% (Schering-Plough).

[c] Warner-Lambert is accruing $134.3 million of one-time charges in 1981. Excluding the effect of these write-offs, the Consumer Sensitive segment's rate of increase in pretax earnings would be 13.59% and 16.84% in 1981 and 1982, respectively.

E = Morgan Stanley Research Estimates

1980. Most observers consider 15 to 20 per year a realistic target, in view of history and the current backlog on file.

Both new FDA Commissioner HAYES and Secretary of Health and Human Services SCHWEIKER are on record supporting a much faster pace of drug approvals. Congressmen GORE and SCHEUER, noted liberal Democrats, recently sponsored legislation aimed at accelerating the pace of new-drug clearances. Congress is now holding hearings on the proposals (we recently attended one and were impressed by how rapidly the message of the 1980 elections has sunk in). We anticipate that the legislators will actually help, not hinder, SCHWEIKER and HAYES in spurring the FDA bureaucracy into action.

Also, there is a remarkably large backlog of drugs now awaiting approval. As **Table 2** shows, the leading United States drug firms now have some 40 completed new-drug applications (NDAs) for completely new chemical entities on file pending Government action (plus many more NDA submissions for combination products, new dosage forms, or additional claims). Foreign drug manufacturers who sell here probably have another 20 to 30, at least. We think it is possible that to clear up this backlog, the FDA will speed up the review of completed NDA submissions. If this occurs, it is conceivable that the number of approvals could spurt to 25 or more in 1982 and 1983, which would stimulate unit volume growth in the United States market.

Table 4. New Chemical Entity NDAs with Very Large Commercial Potential Now Awaiting United States Approval

Company	Drug	Field of Therapy	Why Unique	Estimated U.S. Sales ($ Millions) 1982	Estimated U.S. Sales ($ Millions) 1985
Johnson & Johnson	*Ketoconazole*	Fungal Disease	Superior efficacy	$60	$150
Lilly	*Opren*	Arthritis	Once a-day dosage No G-I side effects May induce remission	50	150
Lilly	*Moxalactam*	Antibiotics	Superior efficacy	60	150
Marion	*Cardiem*	Cardiovascular	Superior efficacy	15	100
Merck	*Blocadren*	Cardiovascular	Same as other beta blockers, but may also be labeled as protective against heart attacks	30	125
Merck	*Moduretic*	Cardiovascular	Comparable efficacy but less toxicity	30	100
Merck	*Ivermectin*	Anthelmintic (animal use only)	Superior efficacy	40	100
Pfizer	*Procardia*	Cardiovascular	Superior efficacy	40	125
Pfizer	*Feldene*	Arthritis	Once a day dosage	90	150
Pfizer	*Celobid*	Antibiotic	Superior efficacy	30	100
Searle	*Verapamil*	Cardiovascular	Superior efficacy	45	125
Upjohn	*Xanax*	Psychopharmaceutical	Possible dual claim for anxiety and depression	25	100

Morgan Stanley Research Estimates

Assessing the NDAs now on file, certain drugs have especially promising prospects. In our opinion, the applications for products with the greatest relative commercial potential and impact on earnings are those of Johnson & Johnson, Eli Lilly, Merck, Pfizer, and Searle. This evaluation is an important factor in our purchase recommendations on the last four issues. As highlighted in Table 4, the specific drugs with the most exciting commercial prospects are Pfizer's *Procardia, Feldene,* and *Celobid,* which together could generate more than $100 million in incremental sales for the company domestically next year (and more overseas); Merck's *Blocadren, Moduretic, Ivermectin,* and *Tocainide,* which have a similar or greater composite potential; Lilly's *Opren* and *Moxalactam,* which are expected to add at least $100 million in sales in the United States (and more overseas); Johnson & Johnson's *Ketoconazole,* a breakthrough improvement in fungal disease treatment with long-term commercial potential in the $100 million or greater range; and Searle's *Verapamil,* which we forecast will be the most heavily used calcium antagonist by 1984 or 1985. The calcium antagonists are the next major wave of cardiovascular treatment agents and, in our opinion, will represent a domestic market of $250 million or more (and worldwide volume of $1 billion) by 1985.

We also expect the domestic volume gains forecast for 1981 and 1982 to be accompanied by margin expansion. Profitability of drug sales in the United States is improving currently (and should continue to do so for the next several quarters) because higher prices are more than offsetting inflationary cost pressures. The gross margin is gradually increasing, and SG&A costs should only rise about 11 to 12 percent this year and next (i.e., less rapidly than revenues). In summary, we forecast domestic pretax profits will grow about 20 percent in 1981 and 21 to 25 percent in 1982. Since the composite (i.e., domestic plus foreign) profit gains projected for the industry are considerably lower (12 percent) in 1981 and somewhat smaller (19 percent) in 1982, it is clear that we anticipate international earnings will expand much more slowly than those from domestic sources and also less rapidly than the historical 15 percent per annum trend.

Part 2 of this report will appear in the September *MM&M.* Included will be discussion of the years 1981 to 1982 – the international market outlook, who will register the strongest gains, which firms could provide profit surprises – along with analysis of the longer-term outlook.

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ATTACHMENT "A"

Generic Pharmaceutical Industry Association

600 Third Avenue, 18th Floor
New York, New York 10016
Telephone (212) 490-8028

FACT SHEET ON PATENT EXTENSION (H.R. 1937)

- The top selling drugs in America are realizing actual legal patent protection for an average of 18.5 years. (See page 2)
- The U.S. pharmaceutical industry is one of the most profitable of all manufacturing industries and "continues to enjoy high and stable profits in terms of return to stockholders' equity."
- "Revenues of the pharmaceutical industry have increased steadily and the relationship between revenues and R&D expenditures has remained stable."
- "Research-intensive companies are committing increasing amounts of funds toward pharmaceutical R&D, and therefore, the potential exists for major pharmaceutical discoveries."
- The Administration is committed to reducing unnecessary regulatory requirements. FDA is already trying to expedite its approval of new drugs and "the duration of the drug approval process may therefore stabilize."
- Patent extension will delay competition and deprive consumers and government purchasers of the savings they can realize with identical, but lower-priced generic drugs.
- The costs of patent extension will fall heaviest on young and middle income families, on the nation's elderly and the chronically ill.
- The benefits of patent extension "will accrue to a few firms" which are already among the most profitable multinational companies in the world.
- The evidence available "neither supports nor refutes the position that innovation will increase significantly because of patent term extension."

NOTE: All quotes are from Patent Term Extension and the Pharmaceutical Industry, Office of Technology Assessment, Congress of the United States. 1981.

Drug Patents Exceed the Statutory Maximum

The stated rationale for patent extension legislation (HR 1937) -- that the federal regulatory process has reduced effective patent life for pharmaceutical products to only 9.5 years -- is not supported by the facts.

The U.S. patent holders of the most frequently prescribed drugs in America, with annual sales of $1,371,000,000, are realizing legal patent protection for an average of 18.5 years

DRUG PRODUCT	1980 SALES* (millions)	NDA APPROVAL	PATENT EXPIRATION	YRS. MARKET PROTECTION
Tagamet (Cimetridine)	$233	1977	1993	16
Valium (Diazepam)	220	1963	1985	22
Inderal (Propranolol)	179	1967	1984	17
** Aldomet (Methyldopa)	133	1962	1984	22
Keflex (Cephalexin)	131	1971	1987	16
Clinoril (Sulindac)	115	1978	1989	11
Indocin (Indomethacin)	75	1965	1981	16
Naprosyn (Naproxen)	75	1976	1989	13
Aldoril (Methyldopa w/ Hydrochlorothiazide)	58	1962	1981	19
Diabinese (Chlorpropamide)	53	1958	1984	26
Mellaril (Thioridazine)	50	1959	1983	24
Zyloprim (Allopurinal)	49	1966	1986	20

AVERAGE YEARS OF MARKET PROTECTION: 18.5

Total Sales Volume, 1980: $1,371,000,000

* IMS DATA

**Motrin, the 4th ranking drug in America, is licensed by the British patent holder to a U.S. company.

The Pyramiding of Drug Patents

The claim that prescription drugs realize only 9.5 years of patent protection is based on a four-page magazine summary * of an analysis which is seriously flawed in methodology: the authors calculate effective patent life by measuring from the date of the earliest patent issued. Their analysis does not take into account the pyramiding effect of subsequent use, process, or other patents which extend patent terms and prolong monopoly life and premium pricing of prescription drugs.

The authors of this much-quoted article have further understated actual patent life of pharmaceuticals by limiting their analysis to New Chemical Entities (NCEs) and excluding all other drug products. OTA acknowledges this flaw in its report on patent extension.

> "By focusing on NCEs, the most extreme reductions in effective patent terms can be determined, but these effects are not representative of the average effects for all new pharmaceuticals."

It should also be noted that while the four-page magazine article has been cited as the basic -- if not sole -- justification for patent term extension, the full analysis is not yet issued, has not been submitted to the sponsoring agency for review, and is not available for independent verification.

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* Research Management, January 1981. "The Decline in Effective Patent Life of New Drugs," a four-page article by Martin M. Eisman & William M. Wardell.

Is Innovation Declining?

Another underlying premise of the pending patent extension legislation -- that pharmaceutical innovation is declining -- is not supported by the findings of the Office of Technology Assessment:

- "Competitive pressure for innovation has not diminished."
- "The relationship between revenues and R&D expenditures has remained highly stable over the past 15 years."
- "Many research intensive firms have indicated that they are increasing R&D expenditures."

Although the number of NCE approvals is an incomplete measurement of innovation, OTA uses this method to determine trends in the industry. Data provided OTA by the Food and Drug Administration shows that the number of NCEs approved in the 8-year period from 1972 to 1980 increased significantly over the number approved in the previous 8-year period:

APPROVED NCEs

	1963 to 1971	1972 to 1980
Totals:	136	175

More importantly, OTA found that "approvals of NCEs offering important or modest therapeutic gain have remained relatively stable."

The Costs and Benefits of Patent Extension

"The price of drugs whose patents are extended will be higher during the extended period than they would have been if patent protection ended." *

"Competitive pressures on patented drugs from generically equivalent drugs will be delayed and in some cases prevented by patent-term extension." *

Since 84% of prescription drug purchases are paid by consumers and not by third-party reimbursement programs, the additional costs of patent extension will fall heaviest on the elderly, the chronically ill, and on young and middle income families. **

* OTA Report.

**See comparative prices and projected annual savings that can be realized with identical generic products, pg. 8.

"The bulk of revenues generated by patent-term extension will accrue to a few firms who have developed financially successful drugs." *

The American Association of Retired Persons and the National Retired Teachers Association summarized the cost/benefit relationship of patent extension in a statement submitted to the Senate Judiciary Committee: **

> "We can be sure that additional years of patent protection will result in very real income transfers from elderly consumers to large brand-name manufacturers."

While the Report of the Senate Judiciary Committee made note of the support from AARP/NRTA of "the concept of patent restoration," it failed to cite the Associations' expressed concerns and recommendation:

> "Enactment of patent restoration will likely result in additional increases in the elderly's expenditures for prescription drugs."
>
> "We are concerned about the effect patent restoration would have on competition in the drug industry, particularly price competition, and whether the benefits of patent term restoration are commensurate with the costs such legislation would necessarily entail."
>
> "Finally, our Associations recommend that alternative approaches to further drug research, development and innovation be explored with the aim being to find alternatives to prescription drug prices as a means of financing R&D."

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* OTA Report.

** Statement of the National Retired Teachers Association and the American Association of Retired Persons on S.255, the Patent Term Restoration Act of 1981, Submitted to the Committee on the Judiciary, United States Senate, April 30, 1981.

The Case for Patent Extension - Fact or Fiction?

The arguments for patent extension are based, according to OTA, on "a widespread belief" that the return to R&D investment is declining.

OTA, however, finds that there is not sufficient data to prove the accuracy of this widespread belief, and concludes:

> "Many factors that influence R&D decisions appear to favor innovation: the industry continues to enjoy high and stable profits in terms of return to stockholder's equity; research techniques have improved; and competitive pressure for innovation has not diminished."

The "problems" which HR 1937 is supposed to remedy may in fact, therefore, not really exist:

- Drug products, as shown, frequently have effective patent lives in excess of the 17-year statutory maximum.
- "The duration of the FDA regulatory procedures may be stabilizing" according to OTA, and the Agency "is now giving highest priority to the drugs that it believes will provide significant therapeutic advances. . ."
- "Pharmaceutical companies earned the fourth highest return on equity in American industry last year, at 20.5 percent, ranking behind the oil services industry, energy companies and the tobacco industry." *
- "There is a remarkably full research pipeline. Almost every major drug firm is now increasing its research and development spending as a percentage of sales, reflecting a high degree of confidence in the prospects for commercial success of products not yet introduced." **

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* The New York Times, "The Drug Business Sees a Golden Era Ahead," May 17, 1981.

** Medical Marketing and Media. "The Drugs in the Eighties: The Growth will be There-Part I," August 1981.

The Generic Drug Industry

Competition from the generic drug industry has significantly reduced the cost of prescription medicine.

The Federal Trade Commission estimated in 1979 that "between 42.1 percent and 74.3 percent of the wholesale price of branded drugs could be saved by the dispensing of nonbranded products instead of more expensive branded drugs." *

For the nation's elderly, who pay 25 percent of the national drug bill, price competition can be a life or death matter. Some 70 to 75 percent of drug misuse among the elderly is due to under-utilization because they cannot afford the medicine that has been prescribed.

Despite the savings that can be realized by the use of identical, but lower-priced generic drugs, 80 to 85 percent of the drugs having generic competition are sold by the large pharmaceutical companies.

Even after patents expire, branded products enjoy what OTA calls "post patent exclusivity," a further extension of market share and monopoly pricing. One study cited by OTA showed that after patents expired, each of 12 major drugs (including Librium and Darvon) retained more than a 90 percent share of the drugstore market and more than an 80 percent share of the hospital market.

Patent extension will provide additional opportunities to extend monopoly pricing periods beyond the 17-year statutory patent term. The members of the GPIA believe that patent extension will delay or preclude the entry of generic drugs into the market, eliminate the competition they provide, and force consumers and government purchasers to pay higher prices for prescription drugs.

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* OTA Report.

COMPARATIVE GENERIC/BRAND NAME DRUG PRICES

Generic (Brand Name) Drug Products	Generic* Price	Brand* Price	Brand Price Times Greater	Annual** Brand Drug Expenditures (millions)	Equivalent Generic Cost (Col.5 ÷ Col.4) (millions)	Possible Generic Savings (Col.5 - Col.6) (millions)
Dipyridamole (Persantine) 25 mg./1000s	$23.75	$108.34	4.6	$58,937	$12,812	$46,125
Isosorbide Dinitrate (Isordil) 5 mg./100s sublingual	1.46	5.41	3.7	54,102	14,622	39,480
Amitriptyline HCL (Elavil) 25 mg./1000s	17.71	73.53	4.2	29,613	7,051	22,562
Chlordiazepoxide HCL (Librium) 10 mg./500s	5.63	43.65	7.8	27,675	3,548	24,127
Tolbutamide (Orinase) 0.5 gm./1000s	42.67	91.58	2.2	22,637	10,290	12,347
Hydralazine HCL (Apresoline) 25 mg./1000s	11.74	66.07	5.6	22,441	4,007	18,434
Isoxsuprine HCL (Vasodilan) 10 mg./1000s	22.72	137.74	6.1	19,101	3,131	15,970
Meclizine HCL (Antivert) 12.5 mg./1000s	8.73	61.76	7.1	17,173	2,419	14,754

TOTAL POSSIBLE GENERIC SAVINGS: $193,799,000

* 1981 Redbook Prices
**1980 IMS Data

Mr. GORE. Well, thank you, Mr. Haddad. You describe the grim picture in which generic drugs encounter all kinds of barriers to market entry from every conceivable direction. How come then generic drugs are capturing an increasing share of the market, are they not?

Mr. HADDAD. Yes. We were very successful in passing a law in many States which finally repealed the antisubstitution law that PMA offshoot passed in the fifties. That law prohibited substitution and advertising of comparative prices. The Supreme Court knocked down the advertising barrier, and State by State we overturned the antisubstitution laws. We now have laws that permit substitution.

They we had Caspar Weinberger's insistence that medicaid pay only the lower generic price for drugs. However, most States with maybe four or five exceptions, have erected administrative barriers to prevent a free flow of generics. In one State, the commission to approve drugs meets every 6 months. In another the commission has been abolished and no replacement approved. In Texas you have to hire a distributor to sell your drugs. Antisubstitution laws helped us as Lou Harris learned in a poll that indicated the average American has gone from 9 to 70 percent in his understanding that generics are not only safe and equal, but cost less.

But you must remember it is still the doctor who prescribes and the patient pays, but the patient now knows because of the kind of confrontations you and Mr. Walker had this morning, they realize it is the same drug and are putting pressure on the doctor to prescribe generically. Yet, 1 out of every 2 drugs that could be sold generically is not sold generically, and 8 to 9 of every 10 consumers pays the higher price for an identical drug.

Mr. GORE. Mr. Clement.

Mr. CLEMENT. Could I have your first chart back up there, please? The 18.5.

Mr. GORE. I think that others will have an easier time seeing it if you put it——

Mr. HADDAD. Put up the generic one alongside there.

Mr. GORE. Let us just put that one up there for the time being. This is on page 2 of attachment A.

Mr. CLEMENT. I am interested in the drugs that you have on there. I do have a question. Considering the legislation that is the vehicle for this hearing, H.R. 1937, can you tell me, Mr. Larsen, would any of the drugs that are shown on that chart be covered by the provisions of H.R. 1937?

Mr. LARSEN. I would have to take a look at each one of them and see. I think the question is the distinction between the bill in the Senate and House.

Mr. ENGELBERG. Certainly the bill that passed the Senate would apply to any drug for which a new use or indication was found. I cannot see the list very well.

Mr. CLEMENT. But those have all been approved?

Mr. ENGELBERG. Approved, but approval for a single indication, so that if someone now finds a new use for that drug which subjects that drug to a new round of NDA approval, presumably the extension bill would apply to that.

Mr. **Larsen**. As an example, we suffer from the same problem. If one of these drugs were found that would help us grow hair again——

Mr. **Clement**. Mr. Larsen, you just found the weak point in the armor.

Mr. **Larsen**. Well, we share the problem.

Mr. **Gore**. In fact that is significant because supplemental NDA's are extremely common, is that right, for new uses?

Mr. **Engelberg**. I cannot speak to that. In the bill passed by the Senate, what would be extended is the patent claim, and whatever extension was granted would be for the product subject to regulatory review for all uses.

Mr. **Haddad**. The difference is Dr. Wardell was talking about the first indication, not all these overlapping, interlocking, stretching patents.

Mr. **Clement**. But in fact these drugs are now as I understand, in public demand; is that correct? Most of them?

Mr. **Engelberg**. No.

Mr. **Larsen**. Take a look at the patent expiration date. Tagamet is 1993.

Mr. **Haddad**. You mean the PMA list.

Mr. **Larsen**. About the only one on that list at this time would be Indocin, and that was effective in January, I believe, of this year.

Mr. **Clement**. But in fact almost all of these drugs that are on your list of those that had—you say 18.5 years of patent protection—virtually all of them originally came in for their NDA—their IND's many years ago, did they not, if I look at your list correctly?

Mr. **Larsen**. Sure.

Mr. **Clement**. Let us——

Mr. **Larsen**. I do not know what the IND date was, but you can look at the NDA approval date and back up from there. You can take a look at every drug on the list and if you would compare with other sophisticated countries in the world as to which ones are still covered by patent, you will find relatively few of these. The only one that occurs to me that would still be covered on this list would be Tagamet, and all the rest in other sophisticated countries are off patent.

Mr. **Clement**. Let me go through some of the drugs on here to see if they would have received any benefit from H.R. 1937 had that bill been public law when they are approved—for example, Valium—would it have received any restoration benefits had 1937 been in effect when it was approved?

Mr. **Larsen**. One of our problems is that you are asking a question that would be nice to answer, but we do not have substantive detail in terms of what the secondary claim might be, because you are talking about another use or application as it may relate to a drug.

Mr. **Clement**. I do not want to go the long way around.

Mr. **Engelberg**. I think the answer is no for its original indication, but that does not preclude the fact that it could have gone through the process more than once.

Mr. **Clement**. Mr. Chairman, perhaps I could go a step further. This list you have used before, or this list of drugs.

Mr. LARSEN. Yes.

Mr. CLEMENT. I took the liberty of asking your opponents on this issue, PMA, to take a look at that list for me to give me an indication of what their analysis was. Mr. Larsen, since I am afraid I offended your sensibilities earlier, this chart was definitely prepared with the assistance of PMA. And it was off center, also.

Now, this chart is basically your earlier chart but it has been reordered in just a descending list starting with the newest approval and going back, and it adds a new final column which I will give my chairman.

Mr. HADDAD. Basically you are saying that the later drugs have less patent life.

Mr. CLEMENT. That is exactly what we are saying. Having taken a look at this, it appears to me that there does not seem to be any question that the drugs that have been approved by FDA within the last 5 years all have less than 17 years of patent life remaining when they get approval to go on the market. In fact, the most recently approved one only had 11 years, and it seems to me that that seems to indicate precisely what the research-intensive firms are saying.

Mr. LARSEN. As I cited for you, a series of patents on Zyloprim and Methyldopa, to analyze this we would need to look at what is the total patent profile on the product. Were you to say the real world is now and let us say that we were into the House bill as it is perceived and you come along with another use and there is another period of time in which it is at the FDA, that other use is going to get the benefit of that extension.

Mr. CLEMENT. Let me ask you something, Mr. Larsen. If you have a drug that has been approved and the 17 years has run, now I understand that the members of your organization do some research, certainly much less than the intensive research done by the other companies.

Mr. HADDAD. Mr. Clement, could I clarify something?

Mr. GORE. Let him finish the question first.

Mr. CLEMENT. Say one of your researchers found a new use for a drug compound that was already in the public domain, could you not then file a new patent application on that new use?

Mr. LARSEN. I suppose that we could.

Mr. CLEMENT. Could you not then get the 17 years?

Mr. LARSEN. 17 years?

Mr. CLEMENT. The less than 17 by the time you receive approval.

Mr. LARSEN. You are talking about a brandnew entity now.

Mr. CLEMENT. No; I am talking about a new use that your researcher would discover on a drug that had been previously approved but had entered the public domain.

Mr. LARSEN. Are you saying under the bill we would receive 17 years from the date of our patent, just as a figure of speech, or are you saying under the provisions of the bill we would receive an extension for the amount of time lost at the FDA?

Mr. CLEMENT. No. The question is, at this point, and even under the bill, that if there was a drug that someone else had discovered and had patented and their patent had run and the drug was now in the public domain and one of your researchers should stumble upon a new use for that drug, would you not then not be free to file a patent application on that new use?

Mr. ENGELBERG. Provided it meets the standards of patentability.

Mr. HADDAD. OTA pointed out only a few companies would benefit from this legislation. In the text of the report they say 11 to 15, and I will use a word not used today, 11 to 15 multinational companies would receive benefit from this legislation, so we are not talking about the 200 members of PMA.

Mr. CLEMENT. I have paid some attention to the frontiers of science, and some of the smaller companies that are going on, and it seems to me that I recall that Genentech, which is hardly a multinational, has appeared before committees of the Congress, and has testified that unless they can get adequate protection for the area in which they are operating, that they may not be able to make it, and there are a lot of small companies out there that count on one or two products, and if they do not get their protection they are going to go under. The entire world is not made of the multinationals.

Mr. HADDAD. I was at every hearing, and I have yet to hear of a second company that was small coming in. We are offended when the Congress puts small business at the top, and we are the small business and we are getting it in the neck.

Mr. CLEMENT. PMA seems to think they are getting it somewhere lower in the anatomy.

Mr. HADDAD. I'm willing to compromise. [Laughter.]

Mr. LARSEN. From my vantage point as one who has been in the industry a long time and one who has a consumer interest as well as a company interest, even though the company is not as big as the one I used to be in, I have a bottom-line interest. I was brought into a company that was virtually on its back to turn it around. We have done it. When one looks at a product with a 26-year period of protection, that is an unreasonable period of time. And if legislation is going to be passed that would enable an extension because of another use coming along or some other effect on any drug, then it would be wrong.

Mr. CLEMENT. Mr. Larsen, you want to talk about the extensions and the pyramiding theory, and I get to a point where I must ask you, can you identify a single drug that cannot be made through more than one commercially feasible process upon the expiration of the initial use patent? Can you think of one?

Mr. LARSEN. You are talking now of the chemical process. Al?

Mr. ENGELBERG. I have not made a study of that particular subject.

Mr. LARSEN. I would say there can be more than one process, but the problem is you get down to what is the economics of the process, and that is the final bottom line of it. If you can produce a product and you cannot compete, you have no product.

Mr. CLEMENT. We just had testimony from one of your colleagues on the panel that your industry is able to sell drugs for one-twentieth of the cost.

Mr. LARSEN. Not that much.

Mr. CLEMENT. Whatever it was, it was certainly significantly less.

Let me just read something that Commissioner Mossinghauf said which gets to the heart of this. I apologize, but it is only a couple of paragraphs. He said before the Judiciary Committee:

> What does a patent on a new use for a product or a new process of making a product convey to the patentee? Regulatory review aside, if the original patent on the product has expired, the public is free to manufacture that product for all the uses for which the product was originally intended as well as for any other use except for the patented one. If a patent for a process or manufacture is also obtained, this particular manufacture is protected, although the public is free to make the product in any other manner. As a consequence, the product itself does not enjoy continued and ever growing patent protection. Lastly, it must be recognized that practical enforcement of use patents and of process patents is difficult. In the case of a protected use, unauthorized substitution is very hard to police. Patents which cover processes for manufacture are equally difficult to enforce. As a consequence

And these are the words of the Commissioner of Patents—

> As a consequence, I find the allegation of patent pyramids difficult to accept, and would tend to favor the view that full protection of a particular product on the market depends upon the product patent itself and upon its effective patent term.

Mr. Engelberg, you have identified yourself as a patent attorney.

Mr. ENGELBERG. Yes, sir.

Mr. CLEMENT. You said you had extensive experience in this field. Do you disagree with the Commissioner of Patents?

Mr. ENGELBERG. With significant parts of it, yes, sir. In my estimate I have identified one situation involving a product patent, not a lesser use or method patent, in which one patent issued at an early date covering a generic group of compounds, of which it turned out cephalexin was a member, and later one covering cephalexin monohydrate, so that the expiration of the first patent does nothing in terms of making the product free to be made by other people. That is one instance.

In terms of method patents, you have the similar generic and specific type of situation where you can get patents first on a broad process and patents on specific and critical improvements. In terms of the unenforceability of use patents in this industry, that is not true, because each use is associated with a different dosage form, different requirements as to how often it has to be taken, and I think it is easy to determine from prescriptions whether or not a particular use is being infringed.

I do recall reading the statement and I do recall that I disagree with substantial parts of it. I might point out another thing, and this relates to the search for information spoken of earlier, and also relates to your question. If you go to find out what you can or cannot do when you believe a product patent has expired and you decide you want to find out if you can for example make librium, you would find there are several thousand patents issued to Roche with no descriptive titles, because the Patent Office does not require specific titles. In order to determine whether or not you can make a particular product you have to spend months and years and money climbing through a lot of patents trying to find out what you can and cannot do. We have heard several times how difficult it would be to conduct a study for the purpose of getting some information for this committee. That same difficulty faces the generic manufacturer every time a patent expires and he begins to think about whether he can make the product without stepping on an insignificant corner of some right.

Mr. CLEMENT. You say that you as an industry spend months going through the Patent Office to determine whether or not you can produce a product and not infringing on a patent. Did they not spend years doing the research to get that patent?

Mr. ENGELBERG. No one is arguing for the destruction of the patent system. We are arguing whether or not the problem of shortened patent life really exists and whether or not this proposed legislation is a fair solution to the problem, and that is what we quarrel with.

Mr. CLEMENT. Let me pose a final hypothetical to Mr. Larsen. You said you took over an ailing company and turned it around and are fighting for your existence. Hypothetically you are the Iacocca.

Mr. LARSEN. I came from Detroit.

Mr. CLEMENT. You have your engineers and they have been working like crazy and they have found the answer. They have something that is patentable. It is going to let every American have the American dream, a 40-foot car that weighs 8 million tons and gets 6 miles to the gallon, but you can dilute the gallon 90 percent with water. It is the answer to the energy problem. You file your patent. You get your patent and EPA and DOE and Interior and everybody else get involved and say they have to check and see if it is safe before you can produce it. And 16 years 364 days later they say, "Larsen, you have got it, you are approved to market it," and the next morning you wake up and open the New York Times and you find out that an Arab consortium knows that it is now in the public domain and they are spending $1 billion promoting this thing, and they can do it, and they did not put a penny into research. Are you happy?

Mr. LARSEN. I think you have to know where we are coming from. In the beginning I said that I personally do not have any quarrel with a guaranteed period of protection. I am concerned about the other side of the responsibility, the responsibility to the consumer. If you are in the generic business, that is where your basic concerns rest, because that is why you exist as a company, because that is whom you are out to serve. That is your niche in the marketplace. So our objective is to more effectively serve that consumer with drugs bioequivalent to the drug that is out there in the first place. We feel that there should be competition. We are saying that as it is presently constituted, there are all of these opportunities for multiple years of protection. We are concerned and we are bringing our concerns to you as a committee that it is unreasonable to think about applying the bill as it is presently constituted and providing even greater extensions. My concern has to do with the process of extension.

I would strongly, as I said in closing my remarks, Mr. Engman spoke with me after we both appeared before the AARP and that he felt it was time to sit down and talk about the bill. In the past, the generic association initiated meetings with PMA. We have been willing but there has been no follow through. The orderly way is to have affected parties sit down together. We want to support the PMA in terms of assuring an adequate return, but we cannot see providing a vehicle that can effectively extend patent protected life beyond reason, as seen in the exhibit.

Mr. CLEMENT. Thank you, Mr. Larsen. I think you have been an exceptionally good witness. I thank the chairman for his courtesy.

Mr. GORE. I promised to invite Mr. Hutt back to join the panel at the witness table.

Mr. HUTT. I suggest in light of the hour and in light of the fact that everyone has covered the same subject at some length, I would be happy to forgo that.

Mr. GORE. That is kind of you, Mr. Hutt. I appreciate it. Thank you all very much. Thank you to this panel and to the other witnesses, and with that the hearing will stand adjourned.

[Whereupon, at 6:15 p.m., the subcommittee was adjourned.]

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